The Royal London

Ophthalmic Hospital Reports.

VOL. XVIII. PART II. SEPTEMBER, 1911.

HERNIA AND RUPTURE OF THE EARLY LENS VESICLE.

By GEORGE COATS.

[PLATE XII.]

FOR this specimen of a very early human fœtus I am indebted to Mr. J. S. Hinnell, of Bury St. Edmunds. The tail-rump measurement was only 4·5 mm., the arms were no more than indicated by minute bosses, and there was no pigment in the pigment epithelium. According to obstetrical calculations the fœtus was supposed to be about 5 weeks old; from the above data, however, three or four weeks is a more probable age.

Owing to an unavoidable delay in fixation the preservation of the tissues was only moderately good. Some of the sections also became torn in preparation, so that it was impossible to make a reconstruction model. The general characters of the abnormality are, however, sufficiently clear. The head was cut in serial horizontal sections.

Fig. 1 represents a horizontal section through the left eye. The lens vesicle (A) is widely open on the surface. On each side the epithelium and basement membrane (or primitive capsule) are fairly well formed. In the centre, however, the capsule is evaginated backwards to form a large triangular cavity (B). The boundary between the lens vesicle proper and this hernial protrusion is sharply delimited on each side

by a little fold of the capsule, which constricts the entrance into the sac. The central cells of the lens vesicle have undergone degeneration and have fallen back into the sac. They have exactly the appearance of the "Morgagnian globules" so commonly associated with the breaking down of adult lens fibres. In the surrounding mesoblast at the apex of the protrusion one or two similar Morgagnian globules are found outside the sac (C). An actual point of rupture in the capsule is not discovered with certainty.

The primary optic vesicle (D) has not undergone invagination to form the secondary. It impinges upon and indents the deep aspect of the hernial sac on one side.

In the right eye there is no hernia, but the lens vesicle is ruptured. It is much better formed on this side, and is nearly closed, a small central opening alone remaining (Fig. 2). Elsewhere the vesicle is closed (Fig. 3), and the posterior cells are already becoming elongated. These posterior cells are often degenerate and vacuolated, and opposite the opening in the vesicle are growing forward in an irregular manner.

Ruptures in the capsule are present on one side. They are mostly small, and some of the cells seem to be finding their way out by a kind of diapedesis (Fig. 2). In the mesoblast in this situation there are a large number of round Morgagnian globules with granular contents (C), and occasionally with a pale nucleus. In this eye also the optic vesicle is uninvaginated; it does not appear in the figures because of the obliquity of the sections.

What would have been the result in this case had development proceeded? The abnormalities already present are: (1) In the left eye a hernia, or, as it might be designated, an enormous posterior lenticonus of the lens vesicle. (2) In both eyes a rupture, or more probably a deficient development of the deep aspect of the lens capsule, whereby some of the central cells were allowed to escape into the surrounding mesoblast. (3) A defective formation of these

central cells, due partly to the escape of some of their number, partly, in the left eye, to loss of support from the ectasia of the lens capsule. In the right eye the abnormality consists in irregularity and vacuolation, in the left it amounts to a total suppression of the cells which ought to form the future lens nucleus.

(1) It is scarcely possible that anything recognisable as a lenticonus would have been produced by the further development of the left eye. With the lens vesicle so greatly deformed it is unlikely that the other parts of the eye would have developed normally; a high degree of microphthalmos with shrunken lens remains buried among persistent mesoblast would probably have been the final outcome. Nevertheless the case shows that Mr. Collins is correct in stating that a protrusion at the posterior pole of the lens may be a pure malformation and not the result of the swelling of lens fibres, or of the traction of the hyaloid artery and its mesoblast—factors to which, according to alternative views, lenticonus is usually attributed* (*vide* Patry, Sur l'Histolog. et l'Étiolog. du Lenticône postérieur. Genève, 1906). In the present instance the swelling of lens fibres cannot have been the cause, since the vesicle is freely open on the surface; nor the traction of the hyaloid artery, since the mesoblast is still undifferentiated.

(2) With regard to the gaps in the lens capsule, these are often found, whether as a primary or secondary lesion, in cases of lenticonus, and also in cases of extensive persistent hyaloid remains. In the present instance, however, since they occur before the hyaloid artery has been formed, and, in the right eye, without associated lenticonus, they seem to be pure developmental defects independent of both these conditions.

(3) Hess, as is well known, has attributed certain types of cataract to disease or suppression of the cells which line the posterior aspect of the lens vesicle, and which should form the nucleus of the adult lens. The types in question

* I do not mean to imply that lenticonus is never due to these causes.

PLATE XII.

FIG. 1.— × 150. Horizontal section through the left eye. A, lens vesicle ; B, hernial sac ; C, degenerate lens fibres (Morgagnian globules) in the mesoblast outside the sac ; D, uninvaginated primary optic vesicle.

FIG. 2.— × 150. Horizontal section of the lens vesicle of the right eye. The vesicle is open on the surface. C, Morgagnian globules in the adjacent mesoblast. About the middle of the left-hand aspect of the lens vesicle a Morgagnian globule will be seen apparently in the act of being extruded through a small opening. The part outside the wall is expanded, the part within it constricted.

FIG. 3.— × 150. A more peripheral section of the same. At this level the lens vesicle is closed and the posterior cells are becoming elongated. They show degeneration and vacuolation, and some of them have escaped into the surrounding mesoblast.

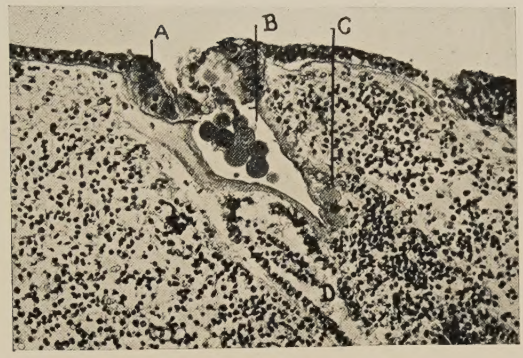

Fig. 1.

Fig. 2.

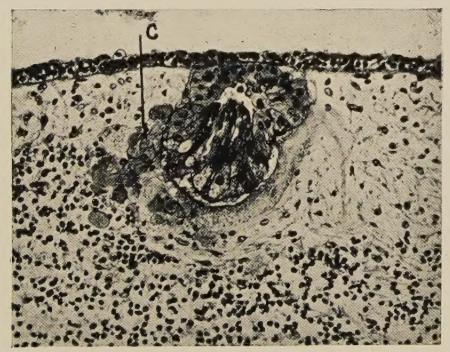

Fig. 3.

Leonardson & Co.

Digitized by the Internet Archive
in 2026

https://archive.org/details/british-journal-of-ophthalmology_1911-09_18_part-2

are "congenital central cataract," in which a spot of opacity is present in the nucleus of the lens,* and what is called by Mr. Treacher Collins "disc-shaped cataract," in which the lens has the biconcave shape of a red blood corpuscle owing to absence of the nucleus, while the peripheral fibres are more or less normally formed.† Hess believes that some forms of congenital lamellar cataract have also a similar origin. He founds his opinions on the examination of a chick embryo of 150 hours in which the lens vesicle still remained widely open, and the cells lining the posterior capsule were breaking down and proliferating freely through the orifice.

The present instance is the first actual proof of the occurrence of this disease and suppression of the lens nucleus in the human eye, but the manner of its suppression is not the same as in Hess's case. There is no evidence that the closure of the vesicle would have been unduly delayed; on the contrary it was almost completed in the right eye. The loss of the nuclear cells was due to their evacuation posteriorly through gaps in the capsule, an occurrence which is mentioned as possible, but rejected as unlikely, by Hess.

* According to Hess, the nucleus may be displaced backwards. This form of cataract seems to correspond with the "discoid" or "Coppock" cataract, of which many cases are reported in recent English literature. Mr. Nettleship (Trans. Ophth. Soc., vol. xxix, Bowman Lecture, p. lxxxi, 1909) considers that the type is "essentially the same" as lamellar cataract, agreeing in this with Hess (*vide infra*).

† For a full description and the literature see a paper by Mr. Treacher Collins (Ophthalmoscope, vol. vi, 1908, p. 669).

THE LACRIMAL DUCTS IN A CASE OF CYCLOPIA.

By George Coats.

[Plate XIII.]

I owe this specimen to the kindness of Lieut.-Colonel H. Herbert, I.M.S.; it includes an area of skin around the fused eyes about 1 inch in diameter, with a corresponding portion of the front of the cranial cavity. The septum between the two orbits has disappeared. The proboscis (P) is connected with a loose piece of bone lying above the fused orbits. Two second, third, fourth, and ophthalmic divisions of the fifth, nerves are present. Of the muscles the external recti alone are distinguishable. The condition of the eyes themselves has been described by me elsewhere (Ophthalmoscope, vol. viii, p. 707, 1910, and vol. vii, p. 732, 1909).

The naked eye appearances are shown in Fig. 1. Owing to the suppression of the parts of the face between the eyes, the two conjunctival sacs have come together and have fused into a single almond-shaped area, the inner ends of the upper and lower lids being displaced upwards and downwards respectively. Each caruncle has been split horizontally, a smaller portion (HC) sharing in the upward displacement of the upper lid, and a large (FC) remaining with the lower. The larger portions meet in the middle line and are partially fused; the smaller are separated by the breadth of the root of the proboscis. Between the partially fused lower caruncles a duct opens, along which a probe can be passed for a short distance only; a trace of mucoid matter escapes from it when pressure is made in the vicinity. All four puncta (C) are present, and approximately in their normal positions.

The ducts of the right side were cut transversely in

vertical serial section; the left lower duct was cut horizontally in a direction parallel to the axis of the canaliculus. The block containing the left upper duct was accidentally lost.

Fig. 2 shows the course of the right lower passages. From the vertical portion of the duct, beneath the punctum (A), two canaliculi (BB) arise. At first the upper is the smaller of the two, but before long they become of equal size, and the upper sinks a little deeper than the lower, lying on its inner upper aspect. Both are perfectly formed and have a normal epithelial lining; in both canalisation is progressing by breaking down of the central cells.

After proceeding for about the length of the normal canaliculus, the two ducts rejoin, forming a single wider tube with much plicated walls (C). This tube sinks sharply backwards, and after a short course runs into a number of loculated spaces (D) lined with two or more layers of epithelium, and representing, no doubt, the cavities of the naso-pharynx. From the same point a tube (E), lined with an epithelium similar to that of the lacrimal ducts, passes forwards with a slightly convoluted course to the external surface, where it opens between the two caruncles in a slit-shaped orifice.

The right upper punctum opens into a flask-shaped dilatation of some size, from the deep inner angle of which a canaliculus of about the normal calibre emerges. After a very brief course the canaliculus turns sharply backwards and enlarges into a cavity with irregularly plicated walls. This cavity comes into communication with the air spaces of the naso-pharynx by means of a slightly constricted opening. The orifices of the upper and lower ducts are entirely separate.

The general course of the left lower passages is similar to that of the right, but there are *two* communications between the ducts and the external surface, a short tube coming off where the duct bends backwards, and opening on the conjunctiva by the side of the caruncle; and a longer

PLATE XIII.

FIG. 1.—Diagram of the macroscopic appearances. P, proboscis; C, puncta; HC, upper half of the left caruncle; FC, partially fused lower halves of the caruncles. Between them a small duct opens. S, an area of thin sclera with the uveal pigment showing through. The corneæ are not visible, being partially buried under the conjunctiva on each side. TC, swollen conjunctiva.

FIG. 2.—Reconstruction of the course of the right lower passages. A, punctum; BB, double canaliculus; C, cavity with plicated walls, probably representing the sac; D, air spaces of the naso-pharynx; E, a tube leading off from the junction of the ducts with the naso-pharynx, and passing forwards to the external surface, where it opened between the semi-fused lower halves of the caruncles.

FIG. 3.—Section of the double canaliculus.

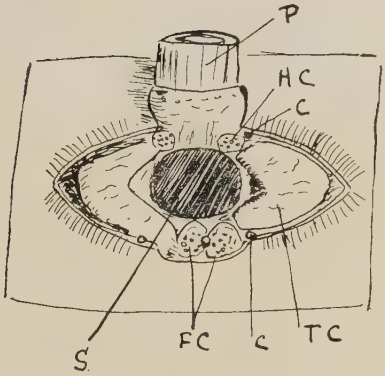

FIG. 1.

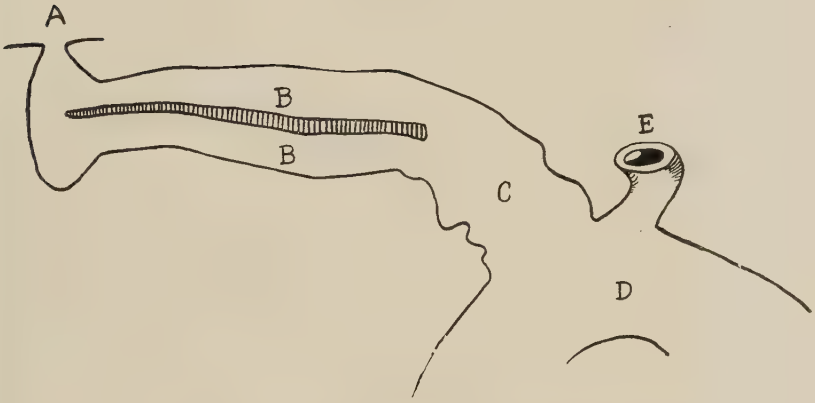

FIG. 2.

FIG. 3.

Leonardson & Co.

one arising at the point of junction of the ducts with the naso-pharyngeal air cavities, and reaching the skin surface at a lower level on the face. These two openings were overlooked in the naked eye examination. On this side the canaliculus is single.

In this instance the lacrimal passages are much better developed than is usually the case in cyclopia. Mayou (Trans. Ophth. Soc., vol. xxvi, p. 270, 1906) found the upper canaliculi and the ducts absent in the four specimens which he examined: the lower were also absent in two. Bock (Klin. Monatsbl. f. Augenh., vol. xxvii, p. 515, 1889) also found puncta only in the lower lid. V. Duyse (Encycl. Française d'Opht., vol. ii, p. 484, 1905) found only the left lower punctum present, the canaliculus ending in a *cul de sac*. In Nieden's case all four puncta were absent (Arch. f. Augenh., vol. xxii, p. 64, 1891). When it is considered that the lacrimal passages normally develop by the formation of an epithelial furrow or strand in the bottom of the groove between the lateral nasal and superior maxillary processes, and that in cyclopia the first named of these processes is divorced from all share in the formation of the groove, being displaced upwards into the proboscis, the astonishing thing is not that malformations should be frequent, but that any approximation to normal development should ever occur.

According to recent researches the lower canaliculus represents the continuation of the naso-lacrimal duct, while the upper is a secondary outgrowth which invades the upper lid (Cosmettatos, Arch. f. Augenh., vol. lv, p. 366, 1906). At first sight it seems inconsistent with this view that in the present instance the upper and lower passages should open quite separately into the naso-pharynx. I believe, however, that in cyclopia the conditions are too complex to admit of deductions being drawn as to the normal course of development. Many of the characteristic features of cyclopia are produced by the meeting of lateral structures

in the middle line and their splitting and displacement, as it were, north and south; in the present case this has happened with the inner ends of the conjunctival sacs and with the caruncles. It is very possible that the lacrimal passages, normally developed up to a certain point, might undergo a similar cleavage and displacement, and so acquire independent openings into the naso-pharynx.

Double canaliculus is not a very rare abnormality. According to Cosmettatos about 40 cases have been recorded, chiefly in the lower lid. Naturally they have been described mostly in cases where the punctum also was double. The two canaliculi may have an entirely independent course to the sac; or they may join before reaching that point; or one of them may have a blind ending; or, the punctum being single, the inner portion only of the canaliculus may be accompanied by a second tube, which has its blind end directed outwards.

The openings beside the caruncles in the present instance are matched by a case described by Schoute (Arch. d'Opht., vol. xxi, p. 320, 1901) under the name "canalicule surnuméraire." These passages, however, and the openings further down on the face, would be better described as congenital fistulæ.

LEUKÆMIC AFFECTIONS OF THE EYE, WITH AN ACCOUNT OF A PECULIAR CASE.

By A. C. Hudson.

[With Plate XIV, Fig. 2.]

The occurrence of ocular complications in the course of leukæmia has long been recognised: as, however, in the majority of published accounts there is a notable absence of detail with regard to the precise character of the associated blood changes, more especially in respect of the relative preponderance of the various types of white cell and the presence of abnormal cells, further data, fuller in these respects, are very desirable for a more precise knowledge of the subject. On these grounds, and on account of the presence of certain very unusual features, the following case seems worthy of record; for the use of the clinical notes on the case, made by Mr. W. Ward, late Senior House Surgeon R.L.O.H., the writer is indebted to Mr. Arnold Lawson :—

Jas. K., *æt.* 36, railway porter, was admitted to the Royal London Ophthalmic Hospital on March 12th, 1910, on account of a tumour of the bulbar conjunctiva of the right eye, which had been noticed eight weeks previously as a slight painless conjunctival thickening to the nasal side of the cornea. The first appearance of the swelling had coincided with an attack of "influenza." The patient had had no other illness, with the exception of a specific affection 14 years previously, and had never been out of England.

On examination: R. eye. The inner and the lower part of the bulbar conjunctiva is involved by a firm brawny pinkish swelling which protrudes between the lids and projects over the nasal border of the cornea. The globe is displaced outwards, and its movement is much impaired. The cornea is bright, and the fundus normal. There is irregular astigmatism

and V. = 6/36, not improved. The right pre-auricular gland is not enlarged.

L. eye. External parts healthy, fundus normal. H.M. 1 D. = 6/6.

In the skin of the right hypochondrium, and also over the left scapula, is a flat oval tumour of rather dusky hue, with many petechiæ on its surface. The tumours appear to involve the whole thickness of the skin, but are movable over the deep parts.

Enlarged bullety lymphatic glands can be felt in both posterior triangles of the neck above the clavicles, in the axillæ and groins, and at the lower border of the right pectoralis minor muscle.

Thorax. The apex beat is situated in the fifth left intercostal space within the nipple line; a hæmic murmur is heard over the pulmonary cartilage. No abnormality is detected in the lungs.

Abdomen. The liver is not enlarged. The spleen occupies the left half of the abdominal cavity, extending down to the pelvic brim and across the mid-line into the right hypochondrium.

The urine contains no albumen and no sugar.

Portions of tissue removed from the conjunctival tumour and the abdominal skin tumour revealed the presence of a leukæmic infiltration which will be subsequently described more fully.

22.iii. R. and L. fundus normal.

24.iii. There is a fresh tumour in the skin over the manubrium sterni.

4.iv. Fresh tumours have appeared in the skin of the chest wall, and over the right scapula, as well as several small nodules in the skin of the scalp. There is also a tumour in the course of the main vessels of the left upper arm, and a nodule beneath the left upper lid which passes back beneath the orbital margin. The tumour over the manubrium sterni has increased considerably in size.

12.iv. There is some diminution in the size of the conjunctival swelling.

X-rays applied for 10 minutes at a distance of 2 feet to the tumour over the left scapula.

23.iv. The tumour over the left scapula, and also the other tumours, are appreciably smaller.

1.v. There is some reduction in size of all the tumours. Spleen as on admission. The patient is considerably weaker.

6.v. Patient short of breath. Pulse 130, irregular, and of poor volume.

9.v. All the tumours are much reduced in size, the conjunctival swelling having almost disappeared. The spleen has become smaller.

There are scattered hæmorrhages, for the most part linear, in both fundi.

18.v. The patient is delirious.

19.v. Patient dyspnœic, pulse rapid and irregular; exitus lethalis.

The temperature during residence in hospital showed an evening rise becoming progressively more pronounced, being not above 100° F. before 10.iv., while after that date it varied between 100° and 103° F., and was occasionally as high as 103·8° F. The normal was not registered after 29.iv., and after 13.v. the temperature was seldom below 100° F. The pulse from 6.v. onwards varied between 100 and 130.

The treatment, apart from the use of X-rays, consisted in the administration of liquor arsenicalis in doses increasing from ♏ v. to ♏ xv. thrice daily. The use of the drug was discontinued on 23.iv., recommenced on 1.v., and replaced on 6.v. by tincture of digitalis ♏ vii thrice daily.

Examination of the blood carried out by Dr. W. O. Meek, of St. Thomas's Hospital, gave the results set out on p. 156.

The following are notes of the *post-mortem* examination which was made 16 hours after death:—

The body is somewhat emaciated. There are tumours in the skin of the chest, back, and inner side of the left ankle, the last-named being of livid hue.

Thoracic Cavity.—There is no accumulation of fluid in the pleural cavities, and the lungs appear normal. The pericardium contains no excess of fluid. There is an ecchymosis beneath the epicardium. The heart muscle is thin and pale. The superior mediastinal glands are enlarged in some cases to the size of a hazel nut, and are somewhat matted. The tonsils appear normal.

	24.iii.	16.iv.	28.iv.	12.v.
Erythrocytes		3,478,150	Anæmia	1,937,500
Hæmoglobin		65 p.c.		20 p.c.
Colour index		0·9		0·6
Leucocytes		67,400	Leucopenia	4,620
Fresh blood		Leucocytes + +		Rouleaux formation. Poikilocytosis.
Stained blood—				
Polymorphonuclear neutrophile cells	307 = 61·4 p.c.	270 = 54 p.c.	205 = 51·25 p.c.	44 = 11 p.c.
Polymorphonuclear eosinophile cells	8 = 1·6 „	2 = 0·4 „	1 = 0·25 „	
Small lymphocytes	10 = 2 „	36 = 7·2 „	21 = 5·25 „	20 = 5 „
Large „	15 = 3 „	37 = 7·4 „	9 = 2·25 „	22 = 5·5 „
Large hyaline cells	97 = 19·4 „	87 = 17·4 „	1 = 0·25 „	3 = 0·75 „
*Atypical ditto			158 = 39·5 „	311 = 77·75 „
Transitional cells	19 = 3·8 „	16 = 3·2 „		
Coarsely granular basophile cells	9 = 1·8 „	4 = 0·8 „	4 = 1 „	
Finely „ „ „	1 = 0·2 „		1 = 0·25 „	
Neutrophile myelocytes	34 = 6·8 „	48 = 9·6 „		
Normoblasts	2 with 500 white cells	4 } With 500 white cells	1 } With 400 white cells	None.
Megaloblasts	Slight polychromatophilia	1 }	1 }	Slight polychromatophilia. Poikilocytosis of red cells. Blood platelets few.

* Large mononuclear cells with more or less round nucleus staining more faintly than that of a large lymphocyte, and with a considerable amount of dense strongly basophile cytoplasm containing vacuoles but no granules. The cells in the last count were larger than in the preceding, and larger than myelocytes. Two of them, one of which has a divided nucleus and is probably about to divide, are shown in Plate XIV, Fig. 2, together with a large lymphocyte, in whose cytoplasm several fine granules are visible, and a polymorphonuclear neutrophile leucocyte.

There are somewhat enlarged matted glands in both posterior triangles of the neck.

Abdominal Cavity.—There is no excess of intra-peritoneal fluid. The spleen is greatly enlarged, weighing 63 ounces; its capsule is much thickened, its tissue tough and dark red in section. There is an accessory spleen, the size of a filbert. The liver is slightly enlarged, but of normal colour and consistence. The kidneys are somewhat enlarged, but are not obviously abnormal on section. The suprarenal bodies and pancreas appear normal. A few of the mesenteric and retro-peritoneal glands are enlarged to the size of a small cherry. There is an ecchymosis beneath the peritoneum of the sigmoid flexure of the large intestine.

The testicles are of normal appearance on section.

The shaft of the right femur contains brownish-red degenerate-looking marrow.

Portions of the various organs, of the conjunctival tumour, and of the skin tumours of abdomen, ankle, and left shoulder, were hardened in formalin and in Zenker's fluid, cut in paraffin, and stained with hæmatoxylin and eosin and with Leishman's stain. The left eye was removed, hardened in Zenker's fluid, and embedded in celloidin. Sections were stained with hæmatoxylin and eosin.

Microscopical Appearances.

Spleen.—The capsule is greatly thickened. The Malpighian corpuscles are unrecognisable. The cells present are entirely mononuclear, possessing in most instances a nucleus which stains like that of a lymphocyte, but varies considerably in size and somewhat in form. It is for the most part round, but forms which present some deviation from a purely round outline are not uncommon. The cytoplasm also varies in amount, having usually the form of a narrow band, while in some cells it is more considerable in amount. It exhibits faintly basophile staining. Cells are occasionally met with having a somewhat more faintly staining nucleus of irregular or reniform outline and a very considerable amount of cytoplasm, in which vacuoles are sometimes visible. The cytoplasm of these cells stains similarly, but somewhat more deeply than that

PLATE XIV.

Fig. 1.—Cells in tissue, and in capillary blood-vessel, of lymphatic gland in case of chloroma. Leishman's stain.

Fig. 2.—Blood film in case of leukæmia. Leishman's stain.

Fig. 3.—Brown line in conical cornea.

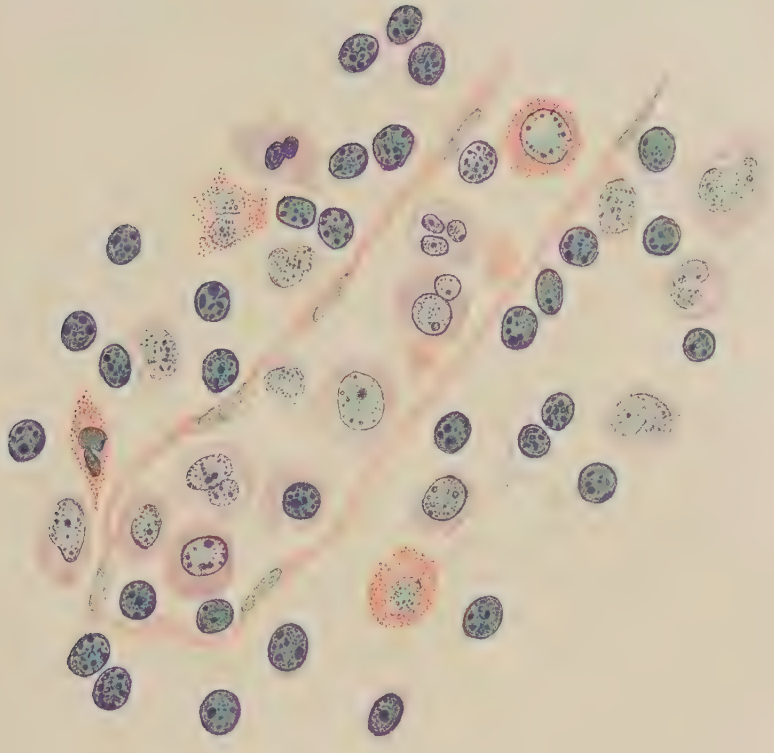

FIG. 1.

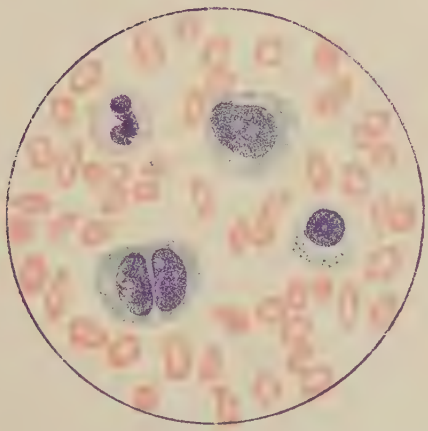

FIG. 2.

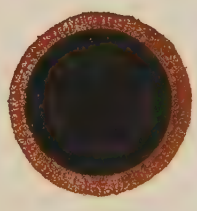

FIG. 3.

Leonardson & Co.

of the smaller cells. The cells themselves appear to be identical with the peculiar large mononuclear cells found in the blood. Cells with much fragmented nuclei in process of degeneration are numerous. Irregularly distributed cells of endothelial type are fairly numerous. Very few cells in process of division, and no granular cells, are seen.

Lymphatic glands.—The cells present are similar to those met with in the spleen; cells with fragmented nuclei are, however, rarely met with. The germinal centres cannot be distinguished, while the endothelium of the blood-vessels is unusually prominent, and scattered amongst the other cells are to be seen cells of endothelial type. The lymph sinuses also contain considerable numbers of large endothelial cells, with large pale nucleus and vacuolated densely staining cytoplasm. Dividing cells are not met with. Polymorphonuclear neutrophile cells may very occasionally be seen in the blood-vessels. Around the gland from the arm there is great excess of fibrous tissue, which, together with the neighbouring fat, is considerably infiltrated with mononuclear cells resembling those found in the gland tissue itself.

The *tonsil* contains cells similar to those met with in the lymphatic glands, cells of the same character being present in considerable numbers amongst the connective tissue fibres of the capsule and the adjacent striped muscle fibres.

Liver.—The capillaries of the liver contain enormous numbers of mononuclear cells, which, except for the absence of cells of endothelial type, are similar to those met with in the lymphatic glands, these cells being present everywhere between the columns of liver cells. Cells of the same character are also seen in the supporting tissue of the portal systems. The liver cells are not degenerated, but contain in some instances golden-brown pigment granules.

Kidney.—The glandular tissue is excessively degenerate, the epithelium of the tubules being swollen, vacuolated, and extensively desquamated. The changes are somewhat less marked in the ducts, while the epithelium of the Malpighian corpuscles is least affected, showing only a moderate degree of vacuolation. The tissues are not infiltrated, but the blood-vessels contain large numbers of mononuclear cells of the same character as those met with in the liver capillaries.

Sigmoid flexure of large intestine.—The mucous membrane is densely infiltrated with cells of the same type as those met with in the lymphatic glands. The epithelium of the mucous glands is exceedingly degenerate, the greater part of it having disappeared. The submucous tissues are free from infiltration.

Bone marrow of femur.—The cells met with here are almost entirely of the same character as those seen in the lymphatic glands and spleen. Very occasionally neutrophile, and still more rarely eosinophile, myelocytes are encountered. The large mononuclear cells, of similar appearance to the peculiar large cells of the blood, are here especially numerous; some of them have an unusually large pale nucleus, and abundant grossly vacuolated cytoplasm.

Skin infiltration from left scapular region.—The epithelium is normal. The connective tissue immediately beneath it contains moderate numbers of infiltrating cells, which, for the most part, lie in the course of the capillary blood-vessels. The infiltration becomes much more pronounced in the deeper layers of the skin, the cells being here aggregated into large areas, which are supported by a scanty connective tissue pervaded by capillaries with richly nucleated endothelium, and from which massive trains of cells pass in all directions into the surrounding tissues. The subcutaneous fat is intensely infiltrated with cells, which separate, often widely, the individual fat cells. The infiltrating cells resemble those met with in the lymphatic glands, the great majority being either of the character of small lymphocytes, or cells with a larger, but similarly staining, more or less round nucleus, which is surrounded by a uniform narrow band of homogeneous cytoplasm. The cells with paler nucleus showing an indentation, and with more voluminous basophile cytoplasm, containing minute vacuoles, are met with occasionally, while cells of endothelial type are also present, sparsely distributed amongst the other cells. In some parts of the infiltration may be seen degenerate red blood corpuscles. A few mast cells are present.

Skin infiltration from ankle.—The epithelium is normal, while the distribution of the cell infiltration resembles that of the skin tumour of the back. The cells of the infiltration also resemble those met with in the latter tumour; cells with a

large, rather pale nucleus, which is seldom round, and often shows an indentation, and with a considerable amount of cytoplasm, which is sometimes vacuolated, are, however, much more numerous. Everywhere throughout the tumour is an extensive extravasation of red blood corpuscles.

Tumour of conjunctiva.—The epithelium is thickened, and in places œdematous, while at other points are small cystic cavities between the cells. The subepithelial tissues are densely packed with infiltrating cells, which separate the connective tissue fibres into a delicate reticulum, supporting numerous capillary blood-vessels. The infiltrating cells resemble those met with in the skin, cells with a nucleus similar to, but larger than, that of a lymphocyte and rather abundant cytoplasm predominating while the mononuclear cells, with more irregular nucleus and vacuolated cytoplasm, are seldom met with. Karyokinetic figures are occasionally seen. In places, masses of mononuclear cells have passed in amongst the surface epithelial cells, and they are occasionally encountered in the cystic spaces met with here.

Left globe: vertical sections.—The anterior parts, including cornea, iris, ciliary body, and lens are normal and free from infiltration. The sclera is also normal. The blood-vessels of the choroid contain a high percentage of large mononuclear cells, but are not abnormally distended; and the tissues are free from infiltration. The retina exhibits an extensive shallow detachment, with degenerative changes in the rods and cones, and exfoliation of the pigment epithelium; these changes are, however, probably of *post-mortem* origin. In the region of the posterior pole are widely scattered hæmorrhages which involve most extensively the nerve fibre and ganglion cell layers. They have apparently arisen in this part of the retina, for the smallest hæmorrhages are limited to it; the larger extravasations have extended into the deeper layers, and have in places given rise to rupture of the external limiting membrane, so that a few red cells are seen in the subretinal space. On the inner side the largest hæmorrhages have caused some separation of the internal limiting membrane. Scattered amongst the red cells of the extravasations are a few white cells of the large lymphocyte type, which show some tendency to aggregation in the central

most degenerate part of the hæmorrhages. At the site of the hæmorrhages the nerve fibre and ganglion cell layers are much disorganised, while both here and in the immediate neighbourhood the nerve fibre layer is œdematous and there is some scattered degeneration of the nerve fibres with cytoid body formation. The tissues of the optic nerve cut in serial section are somewhat œdematous, and there is some scattered degeneration of the nerve fibres. The central vessels are healthy.

The special points of interest in this case consist in the development, in a case which was clinically one of myelogenous leukæmia, of tumours in the conjunctiva and skin, the histological characters of these formations, the presence of fundus changes, and the profound changes of rapid development in the characters of the white cells of the blood, associated with an acute progress and fatal termination of the disease.

Characteristic ophthalmoscopic appearances met with in leukæmia were first described by Liebreich in 1861, and pictured in his atlas. The principal features were summarised as (1) pale colour of all the retinal and choroidal vessels, especially the retinal veins, which, notwithstanding their repletion and tortuosity, have a light pink shade similar to that of the small apoplexies; (2) paleness of the papilla, striated cloudiness of the neighbouring retina, and irregular spots close to the macula; and (3) a number of round, glistening, white spots similar in form and colour to those found in Bright's disease, but differing from the latter in their peripheral situation. In the accompanying sketch, minute hæmorrhages are seen scattered around the macula, in which is a larger hæmorrhage surrounded by a soft white stippling; the fundus is of orange tint. Von Recklinghausen found the white spots in one of Liebreich's cases to consist of varicose hypertrophy of nerve fibres. A similar anatomical basis for white spots observed in the macula in a case of leukæmia was recorded by Roth (Virch. Archiv, vol. xlix, 1870).

Becker (1869) described a case in which the white cells in the blood were more numerous than the red. The eye ground was pale orange yellow. The retinal veins were very broad and of pale rose colour, with indistinct outline; the arteries were narrower, pale yellow in hue, and showed much sharper outlines. The nerve entrance was covered by a fine veil and the retinal tissue in many places, especially next the veins, seemed hazy. There was a brilliant, whitish yellow, prominent spot situated almost exactly in the macula, surrounded by a dark red band, in which were many small, round, also brilliantly whitish-yellow spots. Under observation the red band at the macula disappeared, while the tumour and the surrounding spots lost their brilliance and prominence, leaving a yellowish opacity formed of small yellow spots. At the same time whitish-yellow tumours, surrounded by red bands, appeared in the course of a greatly dilated tortuous retinal vein, which passed upwards and inwards from the optic disc, at a short distance from which it became bordered on each side by a faint yellow band.

Becker described at the same time a second case with enormous increase of white cells in the blood, in which in places the broad, tortuous, rose-coloured veins were edged by a narrow whitish border. He regarded the white masses and the white bands on the veins as due to aggregation of lymphoid cells, and the faint yellow appearance of the retinal arteries as resulting from the excess of white cells in the blood, the peculiar coloration of the fundus being determined by the abnormality of the blood in the choroidal vessels. He inclined to the view that the white mass at the macula originated not in the retina but in the choroid.

Leber (1869), in a case of leukæmia without ophthalmoscopical record, found prominent whitish-yellow foci with red edge in great numbers, especially in the periphery of the retina; in the macula were only some small white spots. The larger foci consisted of lymphoid cells with red cells in great numbers at the edges of the foci. Leber was

of opinion that these corresponded with the ophthalmoscopic appearances described by Becker, and regarded them at first as leukæmic tumours similar to those met with, for example, in the abdominal viscera. He later (1877) discarded this supposition in favour of the view that they resulted from a diapedesis of blood cells amongst which red cells predominated in the earlier, and white cells in the later, stages; but did not exclude the possibility of some local proliferation of the latter.

Reincke (1871) observed prominent foci in the retina similar to those examined by Leber, in which in some cases the red corpuscles in the periphery formed several separate layers, a distribution which the author attributed to a repeated thrusting aside of the hæmorrhage by white cells.

Deutschmann (1878) was the first to describe fundus changes in a case of acute (so-called lienal) leukæmia. The retinal vessels were much distended, but neither they nor the general fundus exhibited a strikingly light hue. There were numerous round and elongated hæmorrhages in each retina, as well as white spots with a red border, the centres of which were found microscopically to consist of crowded leucocytes. In one eye was a milk-white spot just beneath the papilla, which was found to be due to the presence of varicose nerve fibres.

In 1892 the same author described two other cases of somewhat similar character, in both of which there was a high-grade anæmia and leucocytosis. The first case was one of acute lymphatic leukæmia with yellowish discoloration of the fundus, pallor and indistinctness of the optic discs, and numerous retinal hæmorrhages. (The retinal vessels are represented in the sketch as light stripes, showing no distension or tortuosity.) Microscopic examination showed hæmorrhages in the nerve fibre and ganglion cell layers of the retina, overgrowth of the retinal supporting tissue of the optic disc, and infiltration of the walls of the central vein, the optic nerve, and the inter-vaginal space with round cells. The choroidal vessels were packed with leucocytes and the choroid

was slightly infiltrated with the same cells. The retinal pigment epithelium was loosened and slightly pale.

The second case was one of chronic leukæmia in which at first the fundi were not remarkable except for a pronounced tortuosity of the retinal veins. After a few days in hospital however the symptoms became acute, and were associated with a light yellow colour of the fundi, great distension and tortuosity of the retinal veins, and the appearance of several fresh retinal hemorrhages, with whitish infiltrations in the periphery of the retina. Anatomically the retinal and choroidal vessels were found to be enormously distended with leucocytes. In the retinal hæmorrhages the white cells were exceedingly few in proportion to the red cells, while the only change which could be found to account for the white spots was a distended condition of sausage-shaped varicose dilatations of the retinal and choroidal vessels. The retinal vessel walls showed no degeneration. The retinal pigment epithelium was atrophic.

Deutschmann expressed the opinion that atrophy of the retinal pigment epithelium was very essential for the characteristic coloration of the fundus.

Elschnig (1899) described as characteristic of acute leukæmia enormous widening of the retinal veins to five times the normal, with some widening of the arteries, pallor of the blood stream, retinal hæmorrhages, and a peculiar veil-like opacity of the retina which might be present in the absence of other changes.

Murakami (1901), in a case of leukæmia with subacute course and acute termination, found the fundi scarcely paler than normal. The outlines of the optic discs were hazy, the retinal veins tortuous and much distended, and in the periphery of the retinæ were numerous small hæmorrhages, including some with a whitish centre. Microscopically, the retinal vessel walls were infiltrated with leucocytes, and miliary varicosities were found, distended and surrounded by masses of leucocytes, which had given rise to the white spots observed with the ophthalmoscope. There were hæmorrhages

in all the layers of the retina, and œdematous phenomena were much in evidence. Extra-vascular leucocytes in the choroid were few in number. These findings are in agreement with those in one of Deutschmann's cases quoted above and in a case described by Orlow (1903); varicosities in the course of the retinal vessels were also observed by Reincke (1871) and Feilchenfeld (1900).

Grunert (1901), in a case of severe myelogenous leukæmia with papillœdema and hæmorrhages and white spots in the retina, was able to observe the passage of the blood cells in the greatly distended tortuous retinal veins, the white cells exhibiting a slower movement than the red.

Meller (1906) described a case of acute lymphatic leukæmia with no abnormal pallor of the fundus, in which the choroid was found to be densely infiltrated with mononuclear cells, the infiltration extending along the perivascular lymph spaces passing from the eye. Meller regarded this infiltration as of the nature of new growth arising conceivably in the wander cells of the choroid.

Stock (1906), in a case of acute lymphatic leukæmia, found in each eye multiple white spots and hæmorrhages, and a large pre-retinal hæmorrhage between the optic disc and the macula, at the edge of which the retina exhibited a peculiar whitish discoloration which faded towards the periphery of the fundus. At a later stage this discoloration had become less pronounced, while the retinal vessels appeared somewhat fuller than normal, and there was an increase in number of the white spots, some of which lay within the hæmorrhages. Microscopically, in addition to the presence of hæmorrhages, there was found a slight œdema of the papilla, and below it a large focus of retinal degeneration. The choroids were not infiltrated. The author suggested that the yellowish-white retinal discoloration was doubtless due to retinal œdema, and that this was perhaps characteristic of a rapidly progressing stage of leukæmia.

In a case of acute myelogenous leukæmia, in which no ophthalmoscopic examination could be made, Stock found

the retina in the neighbourhood of the macula beset with hæmorrhages, and the choroid around the papilla twice as thick as normal, the whole stroma being infiltrated with large mononuclear leucocytes ; the periphery of the choroid was of normal thickness and free from infiltration. He regarded the infiltration as a result of diapedesis of white cells with possible local proliferation, and was of opinion that the pale coloration of the fundus observed in leukæmia was the result of such infiltration.

Most recently Verderame (1910) has described two cases, one of acute, and the other of chronic, myelogenous leukæmia. In the first case, with a leucocytosis of 240,000 white to 3,700,000 red cells per cubic millimetre, ophthalmoscopic examination showed nothing abnormal beyond the presence of retinal hæmorrhages. Anatomical examination revealed slight œdema of the nerve head and inner layers of the retina, with diffuse sclerosis of the nerve fibres and retinal hæmorrhages. There was no accumulation of leucocytes in the retina, except in the immediate neighbourhood of individual blood-vessels. It is evident, therefore, that the retinal changes corresponded fairly closely with those present in our case. In this case, and also in his second case, Verderame was able to demonstrate the presence of glycogen in the nerve-fibre layer of the retina, in the walls of many blood-vessels, especially in the retina, and in both intra- and extra-vascular leucocytes. In his second case, masses of white cells were found lying on both surfaces of the retina, having broken through both limiting membranes; owing to the histological structure of these masses they were regarded rather as extravasations than as neoplastic formations.

By the courtesy of Mr. J. H. Parsons, we have had the opportunity of examining sections of a very similar infiltration of the retina in a case of acute leukæmia. The infiltration had completely disorganised all the structures of the retina at its site, and projected as an irregular mass on each surface. It was composed almost entirely of cells of

the large lymphocyte type, many of which were completely degenerated, together with a scanty sprinkling of red cells. In no section was a single dividing cell found, and a supporting connective tissue, apart from that of the retina, was completely absent. In view of these histological characters, it is difficult to regard such a cell aggregation as of other than passive origin, although it is not inconceivable that, as the result of unfavourable vascular conditions such as might readily arise in the retina, and of which there was some evidence in this case, a power of active cell growth, which had been evidenced under more favourable conditions, might fall into abeyance. The character of this cell aggregation presented a striking contrast to the infiltration which, in the same case, had involved the posterior part of the choroid. Here both blood-vessels and inter-vascular spaces were densely packed with mononuclear cells similar to those found in the retina; but, in contrast to the findings in the retina, an extremely active cell division was evidenced by the great number of karyokinetic figures seen in the mononuclear cells.

The present state of knowledge with regard to the fundus changes in leukæmia may be thus summarised :—Changes are met with in both lymphatic and myelogenous leukæmia, and in both chronic and acute cases; they are, however, by no means constant, being found, according to Leber, in only one-third or one-quarter of all cases. Both eyes are almost always affected, but not always in equal degree. The changes are, in some cases, limited to the appearance of scattered hæmorrhages, such as were met with in our case, while pre-retinal hæmorrhage may also occur (Stock): in other cases, however, more characteristic features are present, consisting in a light yellowish hue of the whole eye ground; distension and tortuosity of the retinal vessels, affecting more especially the veins, which are of rose tint, while the blood stream in the arteries is abnormally pale; pallor and indistinctness of the optic disc, with a diffuse haze, involving the whole retina, and often more pronounced in the course of the main veins. The

veins may be bordered by white bands, while hæmorrhages are found scattered through the retina, together with white spots which, according to many authors, are more numerous in the periphery of the fundus, so that they may be invisible to ophthalmoscopic examination. Such spots are also met with in the macula; they are not infrequently surrounded by a red border, and may exhibit a definite prominence. Movement of the blood stream in the veins has been observed ophthalmoscopically. It would seem that in the acute cases fundus changes of hæmorrhagic and œdematous origin tend to dominate the picture, while the more characteristic fundus changes have, for the most part, been observed in chronic cases.

Anatomically, the blood vessels of the retina and choroid are found to be distended with blood rich in leucocytes, while hæmorrhages are met with in all the layers of the retina. The white bands bordering the veins are to be attributed to the presence of leucocytes in the perivascular lymph sheaths, while the retinal haze probably results from a diffuse œdema of the retinal tissues. The white areas have been shown to consist in some cases of varicose nerve fibres, and in others of masses of leucocytes, which have been found by some authors to take their origin in varicose distensions of small retinal blood-vessels. The balance of evidence is in favour of diapedesis of cells from the blood-vessels as the main factor in the production of such foci, but the view that some of them are to be regarded as actual leukæmic new growths has recently been advocated by Meller. Anatomical changes in the choroid are by no means constant, but dense infiltration of this tissue with white cells has been described by several authors in both chronic and acute cases, and has been variously attributed to diapedesis of cells from the blood-vessels, with subsequent multiplication in the tissues, extension of extrabulbar infiltration along the perivascular lymph sheaths of the posterior choroidal vessels (Kerschbaumer), and leukæmic new growth (Meller).

The pale colour of the fundus not infrequently observed has been attributed to various causes, namely, high percentage of leucocytes in the blood of the choroidal capillaries, low percentage of hæmoglobin, atrophy of the retinal pigment epithelium (Deutschmann), and infiltration of the choroid with leucocytes. The abnormal tint may, however, be absent in spite of well marked leucocytosis (*e.g.*, in Verderame's case with proportion of white cells to red as 1 to 15), and low percentage of hæmoglobin (Meller, 18 per cent.); and it may be present with a fairly high hæmoglobin content (*e.g.*, 40 to 42 per cent. in Oeller's case). In this last case the light coloration was local in distribution, pointing to a tissue infiltration as the causative factor; it was, however, completely absent in Meller's case, in which dense infiltration of the choroid was found on histological examination. It would seem, therefore, that further data as to the exact nature of the blood changes and the anatomical conditions associated with this phenomenon are necessary before any explanation can be accepted as satisfactory.

It is interesting to note that leukæmia may be associated with vitreous hæmorrhage (Saemisch), while optic atrophy has been found by Oeller, Puccini, and Schultz-Zehden, and optic neuritis and perineuritis by Deutschmann in an acute case. Thrombosis of the central vein of the retina has been described by v. Michel, and changes in the walls of the retinal vessels by Edmunds in a case without precise data as to the blood findings.

The occurrence of leukæmic infiltration in the orbit was first noted in 1875 by Gallasch, who found, in a child suffering from leukæmia, exophthalmos associated with large lacrimal gland tumours. Delens, in 1886, described exophthalmos with multiple tumours in the lids and orbits, the largest of which were in the neighbourhood of the lacrimal glands, in a man of 55 who was suffering from leukæmia. Guaita, in 1890, gave an account of two cases of leukæmia in which diffuse lymphomata of the conjunctiva were present.

The first accurately described case was that of Leber (1878), in which all four lids and the lacrimal glands were the seat of large leukæmic tumours. The patient was suffering from "myelogenous and lymphatic" leukæmia. The examination of the excised conjunctival growth showed a dense infiltration with lymph cells.

In Axenfeld's case (1891) there was infiltration of the lids and tissues of both orbits, especially in the neighbourhood of the lacrimal glands, with pronounced limitation of the movement of the globe.

Kerschbaumer (1895) described a case with decided increase in number of the white cells of the blood, in which both orbits were densely infiltrated with round cells. These passed forwards, in one eye beneath, in the other into, the conjunctiva bulbi, and were continuous along the perivascular lymph spaces of the short posterior ciliary vessels with a similar infiltration of the choroid. Evidence of active cell division in the form of karyokinetic figures was seen in the infiltrations. The external ocular muscles had undergone atrophy with fatty degeneration, while the nerve trunks also showed evidence of atrophy.

Meller, in a case of acute lymphatic leukæmia, found infiltration of the bulbar conjunctiva extending from the upper fornix backwards to become continuous with nodules in the orbit. The infiltrating cells had the characters of lymphocytes and had extended between the cells of the conjunctival epithelium.

The cases of Chauvel (1877), Reymond (1883), and Gayet (1886) not improbably belong to the same class, but the evidence of leukæmia is not definite; while in the cases of Becker-Arnold (1872) and Bernheimer it was absent. Osterwald's case (1881) was almost certainly chloroma.

Leukæmic tumours of the bulbar conjunctiva have rarely been noted. Meller (1906)* described a case of chronic lymphatic leukæmia in which the tarsal conjunctiva of all four lids was involved by a nodular reddish brawny growth, while

* Arch. f. Ophth., vol. lxii, p. 181.

the conjunctiva of the upper fornices was converted into a yellowish, brawny-looking, bloodless mass, of soft consistence. In one eye there was a narrow brawny rampart in the situation of the limbus. There was ulceration of each cornea associated with the presence of ridges in the cornea, which corresponded to blood-vessels and were accompanied by grey streaks; the vessels had no obvious connection with those of the conjunctiva, and their method of distribution resembled that of deep vessels. In another case* of leukæmic infiltration of the ciliary body, simulating intra-ocular tumour, the bulbar conjunctiva, although of normal macroscopic appearance, was found to be infiltrated with cells corresponding in part to the white cells of the blood-vessels; while a pannus-like material was found between the corneal epithelium and Bowman's membrane, which had been partially destroyed. Lymphoid cells had also passed into the deeper layers of the cornea from the neighbourhood of Schlemm's canal. Meller was of opinion that the case described by Henri Coppez† was of similar nature.

The case which presented the closest clinical resemblance to our case is that described by Rollett‡ in which the episcleral tumour formed a reddish-yellow rampart at the limbus, which merged into the conjunctiva above. A small tumour was found upon the sclera at the nerve entrance, and there was lymphoid infiltration of both lacrimal glands. The blood examination showed a slight hyperleucocytosis.

The occurrence in leukæmia of multiple tumour-like nodules in the skin was first described by Biesadecki in 1876. Nicolau (1904) described the occurrence in a case of lymphatic leukæmia of skin lesions of three types: (1) nodules with a strong tendency to ulceration; (2) nodules the size of a pea, with no tendency to ulceration; (3) diffuse swelling and infiltration of the left ear.

* *Loc. cit.*, p. 168.

† Arch. d'Opt., 1895, p. 544.

‡ 10th Internat. Ophthalm. Congress, Section B, 1904, p. 60.

The lobule of the ear was removed and found to be involved by a leukæmic tumour (Prof. Jadassohn). Nicolau was able to collect 10 other cases (Biesadecki, Leber, Hochsinger and Schiff, Neuberger, Hallopean and Laffitte, Nekam, Kreibich, and Pinkus three cases), in all of which the tumours consisted of lymphoid tissue, while the patients were probably the subjects of lymphatic leukæmia. In Hallopean and Laffitte's case there was diffuse swelling of the nose, cheeks, forehead, and upper lip. The case described by Fröhlich (1893), of tumours in three of the eyelids and in the skin in other parts of the body, not improbably belongs to the same group. More recently Lavenson (1909) has reported a case of atypical lymphatic leukæmia with multiple skin nodules, while Rolleston and Fox (1909) have recorded a case of atypical myelogenous leukæmia in a woman of 58, with very numerous plum-coloured nodules in the skin. There was a leucocytosis varying between 730,000 and 33,640 white cells per cubic millimetre, the red cells remaining at about 2,500,000 per cubic millimetre. Myelocytes were present up to 13 per cent. of the total white cells, and there was an increase of the lymphocytes up to 48 per cent., 44 per cent. of which were large. The patient lived eight months after the appearance of the tumours. Improvement in health and a more normal blood count was attributed to the use of naphthalene tetrachloride. X-rays were also employed. This appears to be the first recorded instance of the association of skin lesions with myelogenous leukæmia, and both in the main character of the differential blood count and in the type of the cutaneous infiltrations presents analogies to our case. Fox called attention to the dusky hue of the skin tumours. It seems very probable that in our case this appearance was the result of the extravasation of red blood corpuscles which was observed in microscopical examination of the skin tumours.

As other skin lesions met with in leukæmia may be mentioned erythematous, urticarial, and even bullous

eruptions, and more especially dry scaly lesions resembling pityriasis, which may be distributed all over the body. Rodler-Zipkin (1909) has described a case of this nature in a woman, aged 41, suffering from a large-celled lymphatic leukæmia with acute symptoms. The skin of the whole body was reddened and diffusely infiltrated, the surface scaly and intensely irritable. Anatomically there was found a diffuse infiltration with large mononuclear non-granular basophile cells, affecting in the early stages only the superficial third of the cutaneous tissues, and in the later stages the whole thickness of the skin and the underlying tissue. Mitoses were frequently observed. Rodler-Zipkin has collected six similar cases, in three of which the infiltration was found to consist of lymphoid tissue. A similar involvement of the superficial layers of the skin, associated with intense itching, has been described by Galloway (discussion on Rolleston and Fox's case) in the slate blue maculæ and papules observed in the skin in a case of Hodgkin's disease. The freedom from itching in Rolleston and Fox's and in our case is not improbably to be explained by the deeper origin of the skin infiltration here and the comparative freedom from infiltration of the more superficial and more sensitive structures.

With regard to the genesis of leukæmic infiltrations two main views have been advanced, according to the first of which the lesions owe their origin essentially to a local diapedesis of white cells from the blood-vessels, being thus purely secondary phenomena; while, according to the second, such lesions are to be regarded as a result of stimulation and overgrowth of lymphoid elements pre-existing in the affected tissues. The latter view has been amplified so as to include all forms of lymphoid new formations by Türk, who would explain the varying degree of aggressiveness of such lesions, together with the varying character of the associated blood findings, as dependent on two factors, firstly, the varying grade of local tissue overgrowth, and, secondly, the degree of facility of access of the specific cells to the blood

stream. While in some cases the cell proliferation proceeds slowly, so that the local character of the growth everywhere remains benign, in other cases a more unrestrained proliferation, with implication of neighbouring structures, resulting in a growth of malignant tendency, occurs, these features being in turn modified by the facility with which the specific elements gain access to the blood stream, so that, even in the case of an excessive cell proliferation, tumour formation may remain in abeyance as the result of an excessive flooding of the blood with the new-formed cells. Upon this last factor will also depend the character of the blood findings. Other conditions being equal, facility of access to the blood would appear to be greatest in the case of the lymph glands, spleen, and bone marrow, in accordance with their normal physiological functions. In other tissues, where masses of lymphoid tissue are present in the form of follicles, the facilities for access to the blood stream would appear to be less favourable; this being especially the case when, in regions where, physiologically, only traces of resting lymphoid tissue exist—*e.g.*, the serous membranes and periosteum—as the result of an excessive stimulus an excessive cell proliferation in these minute foci takes place. Under such circumstances it is not surprising that tumour-like foci or diffuse infiltrations of aggressive character should arise.

Meller has accepted this view as to the origin of leukæmic infiltrations not only in the orbit, but also in the choroid, and in some cases (*e.g.*, Feilchenfeld's) in the retina. He is of opinion that the orbital tumours take their origin in all cases from the lymphoid tissue of the conjunctiva or lacrimal gland, their aggressive character being attributable to the difficulty of access of the cells by way of lymphatic channels to the blood stream. He has supported this view as to the neoplastic character of the choroidal infiltrations by the findings in a case of infiltration involving the ciliary region and most anterior part of the choroid, which presented both clinically and histologically

a typical picture of intra-ocular tumour. The case was believed to be one of leukæmia, but exact data on this point are unfortunately scanty. Meller attributed the peculiarly aggressive character of the infiltration in this case, as contrasted with the conditions met with in the more common posterior infiltration, to an obstruction of the lymphatic channels leading from the infiltration. Inasmuch as lymphoid tissue is not present in the normal choroid, this author has suggested a possibility of the origin of the infiltrating tissue from the wander cells normally met with here. Although regarding some of the retinal infiltrations at any rate as of neoplastic character, he is not explicit as to their point of origin. The fact that in Feilchenfeld's case only the membrana limitans externa was broken through by the cell infiltration he would attribute to the absence of blood-vessels, and consequently of perivascular lymph sheaths, which might act as channels of exit for the growing cells from the deeper layers of the retina. Verderame, on the other hand, was of opinion that the masses of white cells which were found in his case of chronic myelogenous leukæmia lying in a groundwork of fibrin on both surfaces of the retina, having broken through both limiting membranes, were to be regarded as of the nature of extravasations rather than as new growths, in view of their relation to pre-existing blood-vessels, coupled with the absence of new vessels and of evidence of cell proliferation. In the case of acute leukæmia in which we have ourselves, as previously mentioned, had the opportunity of examining microscopical sections of the eyeball, the structure of the retinal infiltrations, together with the absence of mitoses in the infiltrating cells, was such as to suggest extravasation rather than neoplastic formation as the cause of the tumours. Kerschbaumer attributed the orbital infiltrations in her case to a diapedesis of white cells from the blood-vessels, and the choroidal and retinal infiltrations to an extension from the orbital infiltration; in this case a local proliferation of the cells was evidenced by the presence of karyokinetic

figures. Stock inclined to a similar view as to the origin of choroidal infiltrations, being unable to accept the possibility of their occurrence as a result of local proliferation of lymphoid tissue. In our case the occurrence of hæmorrhages in some of the tumours (*e.g.*, in the skin) is in favour of a direct origin of the infiltrating cells from the blood stream, while some local proliferation was evidenced by the occurrence of mitoses. We shall subsequently show that these changes are also compatible with a hypothesis as to the genesis of the infiltrations somewhat different from those which have already been referred to.

The onset in the course of typical myelogenous leukæmia of acute symptoms, in association with the appearance in the blood of great numbers of large non-granular cells, as met with in our case, although of rare occurrence, has now been described in a considerable number of cases. Kleinberger (1909) recorded two cases of this character, in the first of which large non-granular cells with a well-staining nucleus and basophile netted cytoplasm came to constitute as much as 75 per cent. of the total white cells of the blood. He regarded them as myeloblasts, following Naegeli, who considers that in these cases, as a result of exhaustion of the blood-forming foci, the blood becomes deluged with immature marrow cells. Rist and Beclére (1910) refer to three cases of typical myelogenous leukæmia in which a sudden exacerbation of symptoms coincided with the appearance in the blood of large round non-granular mononuclear cells, with central or paracentral nucleus, which occupied nearly the whole cell and stained deeply like that of a lymphocyte. The cytoplasm formed a narrow band, and was fairly strongly basophile. The authors, without giving a definite opinion, stated that the cells appeared to be identical with those regarded by many authors as myeloblasts. In our case the cells were characterised by the large amount of basophile cytoplasm, in which vacuoles were often visible. The assumption that they may possibly have had their origin not in the bone marrow, but in the endothelium of the blood-vessels,

lymph glands, spleen, and infiltrated tissues, receives some support from the prominence of endothelial cells in the tissue infiltrations, and the presence in enormous numbers of the mononuclear cells in the capillaries of the liver. On this supposition the increase in the percentage of non-granular cells in the blood, together with the occurrence of the various tissue infiltrations, would be explicable as the result of an attempt on the part of the organism to make good the defective supply of mature granular cells from the marrow by a compensatory proliferation of endothelial cells in various tissues, the resulting new-formed cells being met with for the most part in the blood in a very immature stage, and in the tissues in more mature forms. In favour of such an origin of the large mononuclear cells, as opposed to a myelocytic relationship, is the absence of forms intermediate between them and myelocytes in the blood and in the tissues; nor is the preponderance of the cells in the bone marrow irreconcilable with an endothelial origin. The occurrence of hæmorrhages in some of the infiltrations, *e.g.* in the skin, although suggestive of a tissue infiltration by cells which have gained access from the blood stream, would not be difficult to reconcile with the view which has been suggested above, which would also afford an intelligible explanation of the origin and peculiar characters of the choroidal infiltrations, and a possible source outside the blood stream for those found in the retina. On the other hand, having regard to the resemblance of the large mononuclear cells to those which have been identified as myeloblasts, and their preponderance in the bone marrow, it will probably be wisest to regard them provisionally as of the nature of immature myelocytes. Whatever be the origin of the large mononuclear cells, there can be no doubt that, as pointed out by Rist and Beclére, and exemplified by the cases of Kleinberger and by our case, their appearance in the course of myelogenous leukæmia is to be regarded as of exceedingly grave prognosis. Kleinberger notes that acute exacerbations in the course of myelogenous leukæmia have first been recognised since the general use of

X-rays in treatment, and is inclined on that account to connect the two events as cause and effect. Rist and Beclére, on the other hand, do not consider that this treatment has any influence on the appearance of the large mononuclear cells in the blood; it is, however, notable that in one of their cases the changes occurred during X-ray treatment, while in our case also they were first noted shortly after the application of X-ray therapy.

Bibliography.

General.

Greeff. Lehrbuch d. path. Anat. des Auges, 2nd Edition, p. 382 (with literature).

Groenow. Graefe-Saemisch Handbuch, 2nd Edition, vol. xi (with literature).

Meller. Arch. f. Ophth., 1906, vol. lxii, p. 130.

Parsons. Pathology of the Eye, vol. iv, p. 1317 (with literature).

Türk. Wien. klin. Wochensch., 1903, No. 39.

Fundus Changes.

Becker. Arch. f. Augenh., 1869, vol. i, p. 94.

Deutschmann. Klin. Mon. f. Augenh., 1878, vol. xvi, p. 231.

Deutschmann. Beit. z. Augenh., 1892, iv.

Edmunds. Trans. Ophth. Soc. U. K., 1890.

Elschnig. Wien. Med. Wochensch., 1899, p. 1455.

Feilchenfeld. Arch. f. Augenh., 1900, vol. xli, p. 271.

Grunert. Centralb. f. Augenh., 1901, vol. xxv, p. 125.

Leber. Klin. Mon. f. Augenh., 1869, vol. vii, p. 312.

Leber. Graefe-Saemisch Handbuch, 1st Edition, 1877, vol. v, p. 599.

Liebreich. Deutsche Klinik, 1861, No. 50.

Meller. Arch. f. Ophth., 1906, vol. lxii, p. 130 (with literature).

v. Michel. Deutsches Arch. f. klin. Med., vol. xxii.

Murakami. Klin. Mon. f. Augenh., 1901, vol. xxxix, 1, p. 136.

Oliver. Trans. Am. Ophth. Soc., 1897, p. 212.

Orlow. Medic. Obosr., 1903, No. 3.

Reincke. Virch. Arch., 1871, vol. l, 1.

Roth. Virch. Arch., 1870, vol. xlix, 4, p. 44.

Saemisch. Klin. Mon. f. Augenh., 1869, vol. vii, p. 305.

Stock. Klin. Mon. f. Augenh., 1906, vol. xliv, 1, p. 328.

Verderame. Virch. Arch., 1910, 3, p. 367 (with literature).

Orbital Changes.

Axenfeld. Arch. f. Ophth., 1891, vol. xxxvii, 4, p. 102.
Becker-Arnold. Arch. f. Ophth., 1872, vol. xviii, 2, p. 56.
Bernheimer. 20ste ophth. Versamml. in Heidelb., 1889.
Birch-Hirschfeld. Arch. f. Ophth., 1903, vol. lvi, p. 387.
Chauvel. Gazette hebdom., 1877, No. 23.
Delens. Arch. d'Opht., 1886, p. 154.
Gallasch. Jahrbücher f. Kinderheilk., 1875.
Gayet. Arch. d'Opht., 1886, p. 15.
Guaita. Bericht über den 12sten ophth. Congress in Pisa, 1890.
Hochheim. Arch. f. Ophth., 1900, vol. li, p. 347.
Kerschbaumer. Arch. f. Ophth., 1895, vol. xli, 3, p. 99.
Leber. Arch. f. Ophth., 1878, vol. xxiv, 1, p. 295.
Meller. Arch. f. Ophth., 1906, vol. lxii, p. 130 (with literature).
Osterwald. Arch. f. Ophth., 1881, vol. xxvii, 3, p. 203.
Reymond. Annali di Ottalm., 1883.
Stock. Klin. Mon. f. Augenh., 1906, vol. xliv, 1, p. 328.

Conjunctival Changes.

Meller. Arch. f. Ophth., 1906, vol. lxii, p. 184.
Rollet. 10th Internat. Ophth. Congress, 1904, Section B, p. 60.

Skin Changes.

Biesadecki. Wien. med. Jahrbücher, 1876, p. 230.
Fröhlich. Wien. med. Wochensch., 1893, No. 7.
Lavenson. Univ. Pennsylv. Med. Bull., 1909, vol. xxi, p. 178.
Nicolau. Ann. dermat. et syph., 1904, vol. v, p. 752 (with literature).
Pinkus. Berlin dermat. Gesellsch. in Dermatol. Zeitsch., 1899, p. 361.
Rodler-Zipkin. Virch. Arch., 1909, p. 135.
Rolleston and Fox. Brit. Journ. of Dermatol., 1909, vol. xxi, p. 377.

Blood Changes.

Kleinberger. Deutsch. med. Wochensch., 1909, p. 2161.
Rist et Beclére. Soc. de biol. Paris, 1910, vol. lxiii, p. 429.
Wolfer. New York Med. Journ., 1910, p. 1069 (with abstract of reported cases of acute myelogenous leukæmia).
Zipkin. Berl. klin. Wochensch., 1910, vol. xlvii, p. 2063.

A CASE OF CHLOROMA.

By A. C. Hudson.

[With Plate XIV, Fig. 1.]

The rarity of the occurrence of cases of chloroma is such that the opportunities for studying the clinical and pathological characters of this disease have been comparatively scanty, a fact which seems to justify the publication of any account such as the present one, which may serve to supplement our knowledge, and facilitate the recognition, of the condition.

Kathleen L., *æt.* 7, was admitted to the Royal London Ophthalmic Hospital on May 18th, 1908, under the care of Mr. Arnold Lawson.

According to the father's statement the patient had been suffering for some months from consumption of the bowels; she had been an in-patient at Shadwell Hospital for Children early in the year, for pulmonary tuberculosis. Recently the general health appeared to have improved, but for some weeks a "white skin" had been noticed over both eyes, and for four days the eyes had appeared unduly prominent. There had been no other illness except measles four years previously.

The child was in a very emaciated condition, and looked extremely ill. She was suffering from numerous bedsores, and her clothing was saturated with intensely foul urine. The attitude was apathetic, but any interference provoked a vigorous protest, the mental faculties appearing to be surprisingly little impaired. The complexion was intensely pale, with a faint greenish tint. There was great proptosis of both eyes, with considerable impairment of movement. The corneæ had suffered severely from exposure, almost the entire right and the left in its greater part having become superficially ulcerated; no view could be obtained of the deeper parts, and vision was reduced probably to little more than perception of light. The bulbar

conjunctiva projected as a congested swollen mass between the tense lids, which were involved by a firm deep red œdema passing apparently back into the orbits. There was some ulceration of the skin of the lower lids. The superficial veins of the upper lids and the superficial temporal veins on each side were noticeably distended. Examination in the region of the upper lids revealed no fluctuation, pulsation, thrill, or bruit. The superciliary ridges appeared somewhat abnormally prominent, the left rather more so than the right; examination of the other bones revealed no abnormal thickening. Hearing seemed to be considerably impaired, but there was no ear discharge and no swelling or tenderness in either mastoid region. The head was not retracted. The gums and tongue were covered by a white fur, but there was no evidence of gingivitis, and the fauces and nasal passages appeared healthy. No evidence of disease was detected in the chest. The superficial epigastric veins were somewhat distended, and the abdomen was tumid but free from rigidity or tenderness. There was some enlargement of the liver; the spleen was not felt. The temperature was 98° F.

Chloroform was administered immediately after admission to hospital and a tarsorrhaphy performed on both eyes, an operation which had to be repeated on three subsequent occasions as the tension on the stitches was such as to cause great difficulty in maintaining satisfactory approximation of the lids. On each occasion the blood was noticed to be very thin and dark, and oozing was abnormally free and protracted.

The patient's condition appeared to improve for a time, the appetite becoming better, and the temperature remaining normal. The urine, which was still intensely foul, was passed frequently in the bed; it was found to contain pus cells but no casts, and on cultivation afforded colonies of the colon bacillus. The temperature continued normal until the night of June 1st, when it rose to 103° F., the patient complaining of pain in the left ear. The following day the pain was felt also in the left side of the neck, and there was some discharge from the left ear. Examination revealed a diffuse swelling behind the left mastoid process, with a corresponding well-marked thrill, and a continuous waxing and waning bruit; a similar bruit could be heard

behind the angle of the right jaw. Neither bruit was influenced by compression of either common carotid artery.

On June 4th the left pinna had become pushed forward, and behind it was a red, tender, slightly œdematous swelling exhibiting deep fluctuation. On the following day, on the advice of an aural surgeon, who had, however, had no opportunity of a personal examination of the case, this swelling was incised, and about half a drachm of greenish stinking fluid, of the appearance of thin pus with some stringy flakes, was evacuated. The underlying mastoid process was bare of periosteum, and presented some roughened areas. The temperature, which on the two preceding days had been 102° F., fell to normal the same evening, and the ear discharge assumed a blood-stained character.

On June 7th fine crepitations were heard over the upper part of the left lung. There was a soft enlargement of the liver to the level of the umbilicus; the spleen could not be felt. On the night of the 9th the patient complained of pain in the head, crying out suddenly on several occasions. She subsequently became progressively weaker, and died quietly on the morning of the 13th, the mind remaining apparently perfectly rational to within a few hours of the end. The temperature, which immediately after the mastoid incision had fallen to normal, rose on the following evening to 101° F., after which it showed a gradual fall, attaining normal limits from the morning of the fifth day onwards; the pulse, however, showed no improvement, remaining small and rapid (130–160) from the onset of the acute symptoms until the fatal termination.

The *post-mortem* examination, conducted by Mr. Geo. Coats about 10 hours after death, revealed the following condition :—

Body emaciated; abdomen protuberant; blood pale and fluid.

Head.—Some small sub-periosteal hæmorrhages on the frontal bone on each side of the sagittal suture, and a greenish thickening over the lower part of the coronal suture on the left side. The dura mater, in the course of the superior longitudinal sinus, is stained green, especially posteriorly. There are green patches in the inner wall of the sinus, which contains greenish-red clot, either *post mortem* or not very long *ante mortem*.

From the inner surface of the dura mater of the left middle

fossa, at the level of the middle meningeal artery, a putty-like dark green mass projects. It is not connected with any sinus, and the underlying bone is not eroded. There is a depression of the corresponding temporo-sphenoidal lobe of the brain, but practically no sign of meningitis or encephalitis; the brain is otherwise healthy. There is some green thickening of the walls of the lateral sinus, but no connection between either sinus and the middle ear. On both sides the mastoid emissary vein is as large as a small goose-quill, and on the left side its extracranial portion corresponds with the swelling observed clinically behind the mastoid process. The left petrosal sinus is occupied by green thrombus, and the cavernous sinus by greenish-grey thrombus; the intracranial portions of the internal carotid trunks are healthy. Beneath the periosteum round the left internal auditory meatus, between the right internal auditory meatus and the cavernous sinus, and over the great wings of the sphenoid, are flat green areas. Both petrous bones are infiltrated with greenish material, and the internal ears contain what looks like green pus. The tegmina tympani are intact. Both orbital plates of the frontal bone are infiltrated with green material, but both here and in the other cranial bones, apart from the green discoloration, the cancellous tissue presents no obvious abnormality. Between the roof of each orbit and the levator palpebræ is a brawny mass, quite half an inch in thickness, with a homogeneous dull green cut surface. It is of leathery consistence in its upper, softer in its deeper, part. The orbital contents are fairly normal below, and the optic nerve and globe are not involved in the mass.

Chest.—There is a green discoloration of the posterior surface of the sternum and of several of the ribs, which are also green on section, but free from tumour formation. The thymus is not obviously enlarged. There are a few enlarged glands in the posterior mediastinum. Petechiæ on surface of heart and lungs. Recent fibrinous adhesions at anterior aspect of left lung apex; firmer adhesions at right apex. The lungs are œdematous; no foci of tuberculosis or new growth found. The heart muscle and the valves are normal.

Abdomen.—Liver and spleen enlarged and pale. There are enlarged green glands in the neighbourhood of the portal vein

and along the vertebral column. The kidneys are not enlarged, but contain dark green patches towards their upper part; the patches are not sharply defined, and in some cases the central part is of very soft consistence. The suprarenals are normal. The ovaries are uniformly enlarged, the right being about the size of a plover's egg, solid in consistence, and quite green in section. The pancreas is normal. The bladder appears normal.

Cultures were taken from the following parts:—

Left petrosal sinus (sterile).
Left middle ear (cocci and diphtheroid organisms).
Orbital tissues (cocci).
Green patch in kidney (Bacillus coli).

Sections of the entire contents of the left orbit, roof of the orbit, rib, lymphatic glands, right kidney, and left ovary were stained with hæmatoxylin and eosin after fixation in Zenker's solution and salt formalin. Leishman's stain was also used in the case of the orbital infiltration, lymphatic gland, spleen, kidney, and ovary. In all cases the pathological changes are essentially the same, consisting in a diffuse infiltration of the tissues with a peculiar type of granular cell.

The blood-vessels contain great numbers of cells similar in character to those seen in the infiltrations, and both here and in the tissues karyokinetic figures are to be found.

The following is a detailed description of the changes found in the various organs:—

In the *kidney* the invading cells are met with in all parts, both as a diffuse infiltration and in more localised aggregations, which merge, however, imperceptibly into the surrounding more diffusely infiltrated areas. The character of the infiltrating cells is best seen in the more diffuse areas, where they are found to consist of round cells of about twice the diameter of a red blood corpuscle, having a central nucleus which is in most cases round and about as large as a red blood corpuscle, but is not infrequently oval, reniform, or, rarely, double. Occasional karyokinetic figures can be seen. The nucleus stains deeply, and is surrounded by a somewhat broad band of protoplasm closely packed with minute granules, which exhibit usually neutrophile, but not infrequently eosinophile, affinity; basophile cells are not seen.

The capillary blood-vessels contain great numbers of precisely similar cells, which appear in the sections to form with the red blood corpuscles almost the entire constituents of the blood. Mr. L. S. Dudgeon, who has kindly examined Leishman-stained preparations of this and several other of the tissues, is of opinion that these characteristic cells have all the appearances of myelocytes as seen in the tissues and blood in leukæmia. In addition to the above-mentioned cells there are also to be seen a certain number of ordinary small lymphocytes. In the dense infiltrations the cells appear to be of the same character; they are, however, less well defined, and both the nuclei and cytoplasm more irregular in form, disposition, and affinity for stain, many of the cells being apparently in process of degeneration. The cells are for the most part, but apparently by no means invariably, separated from their neighbours by a fine connective tissue. Some of the large cells which are undergoing degeneration contain pigmented granules, the hue of which varies from dark golden yellow to olive green, and the same process is apparently responsible for the appearance of irregular protoplasm-like masses containing pigmented granules and large pigmented globules free in the tissues. Occasional karyokinetic figures can be seen in the large cells, and some of these have two nuclei. No giant cells and very few plasma cells are to be seen either in this or in the other tissues examined. The glandular tissue has undergone advanced changes, which are most easily seen in the less densely infiltrated areas. Here there is extensive degeneration of the epithelium of the convoluted tubules associated with swelling, the tubules themselves containing a granular or fibrin-like coagulum; these changes are also to be seen in areas free from infiltration. Many of the collecting tubules have also undergone degeneration and contain a hyaline-like material. The epithelium of the glomeruli usually presents a fairly normal appearance, but Bowman's capsule is in many cases greatly thickened and in places the connective tissue of the organs is considerably increased. In the most densely infiltrated areas the renal elements have either completely disappeared or are represented by strands of connective tissue, or by columns of hyaline-like material, evidently the contents of pre-existing tubules.

The cells of the *orbital infiltration* are essentially of the same character as the granular cells found in the infiltration in the kidney, but are somewhat more irregular in size and contour, and in the size of the nuclei. In a small proportion of the cells the nucleus is only about half the diameter of a red blood corpuscle, the cytoplasm containing strongly eosinophile granules; some of the cells of this type show karyokinetic figures. In the peripheral parts of the tumour, in relation to the periosteum, fibrous tissue is present in large amount, and the infiltrating cells are frequently distorted and shrunken, apparently as the result of pressure, the nuclei having undergone similar changes and being not infrequently broken up. In the more central parts the cells are well formed and can be seen very extensively invading the orbital fat and muscles, the individual fibres of the latter being separated and in some cases atrophied; many of the cells contain small golden granules scattered through their substance. Cells with any resemblance to polymorphonuclear leucocytes are exceedingly few. Capillaries and considerably larger blood channels lined by a single layer of endothelium are fairly numerous.

The cancellous spaces of the *roof of the orbit* contain great numbers of the characteristic granular cells lying in a scanty stroma, but the bone itself has not been eroded. Cells with a small, round, densely staining nucleus and a broad ring of granular cytoplasm are numerous here. Occasional karyokinetic figures can be seen.

In the *rib* the cells have similar characters; the periosteum and inserted muscles are also infiltrated by cells which have in most cases a large, rather faintly staining nucleus, and there is some destruction of the muscle fibres.

In sections of *lymphatic gland* the characteristic granular cells are present in enormous numbers, occupying usually by far the greater part of the fields (Plate XIV, Fig. 1). The cells are for the most part similar to those met with in the kidney, but cells with small, deeply staining nucleus and eosinophile granules, of the type met with in the bones, are also present, and karyokinetic figures in cells apparently of this type are not uncommon; such figures in the granular cells contained in the blood-vessels of the organ appear to be comparatively common. The trabeculæ show

some infiltration with the characteristic cells. In association with the above-mentioned cells are ordinary lymphocytes, for the most part sparsely scattered, but occasionally collected into fairly well defined nodules. The central area of several degenerated cells, apparently of the granular type, shows an ill-defined dark green stain, and here and there amongst the cells, and in some cases in the body of large degenerated cells, can be seen masses of granular, dark gold or greenish gold pigment. Polymorphonuclear leucocytes are almost entirely absent.

The *ovarian tissue* has been completely displaced to the margins of the organ by a cellular infiltration lying in a fine stroma containing numerous capillaries and larger blood channels lined by a single layer of endothelium. The cells are similar in type to the granular cells met with in the other organs, the nuclei being, however, for the most part large, round, and faintly stained. Occasional karyokinetic figures are present. Hæmorrhages have occurred in the organ.

Globe.—The cornea is considerably infiltrated. The iris is slightly infiltrated and its root is approximated and probably adherent to the back of the corneo-sclera. The ciliary body, choroid, retina, and sclera are free from infiltration. The papilla is swollen, but not infiltrated. The optic nerve is free from infiltration. The blood-vessels in all parts, but especially in the choroid, contain a large proportion of mononuclear cells with large round nucleus and granular cytoplasm similar to those met with in the infiltrations.

The question of the precise pathological status of chloroma is one which has given rise to much discussion, and will be referred to here only in so far as seems essential to an appreciation of the histological appearances found in the present case. For a fuller consideration, reference may be made to such authors as Klein and Steinhaus, Dock and Warthin, Sternberg, Türk, Treadgold, and Lehndorff. The disease has been described as "Cancer Vert" (Aran, 1854), sarcoma (Virchow, 1869), periosteal sarcoma (Huber, 1878), lymphoma (Behring and Wickerkiewicz, 1882), Chiari, 1883, and Dock, 1893), and recently again round-celled sarcoma

(Hebb and Bernstein, 1909). Waldstein, writing in 1883, was the first to suggest that the disease was of leukæmic nature, regarding the chloromatous tumours as secondary manifestations, a view in which he was supported by von Recklinghausen. Waldstein considered that the primary lesion in his case was probably in the bone marrow, an observation which has subsequently been endorsed by Guembel, Dock and Warthin, and others. Since then the evidence in favour of an origin of the disease in the hæmatopoietic system has been strengthened by the discovery in chloromatous tumours of large numbers of cells of the nature of myelocytes. These appear to have been first observed by Türk, who, in 1902, reported as chloroma the case of a man, *æt.* 38, suffering from leucocytosis (47 per cent. myelocytes, 32 per cent. polymorphonuclear leucocytes, 14·75 per cent. lymphocytes), in which *post-mortem* examination revealed scattered green deposits in the periosteum of the lumbar vertebræ, diffuse uniform grass-green marrow in many of the bones, and grass-green foci in the kidneys. The marrow consisted almost entirely of neutrophile myelocytes, and there were fairly numerous myelocytes in the spleen and in some greenish retro-peritoneal glands. It is interesting to note that nine years previously Dock had observed, amongst the cells of the growth in a case of chloroma, cells in which the nuclei were surrounded by a finely granular protoplasm; mast cells were present in excessive numbers in or near the neoplasms.

Klein and Steinhaus (writing in November, 1903) described the case of a man suffering from an increasing leucocytosis (20,000 to 41,000 leucocytes per cubic millimetre), with high and rapidly increasing percentage of large lymphocytes. Myelocytes varied from 16 to 32 per cent. Many of the bones and viscera were found *post mortem* to be involved by green tumour-like tissue, consisting chiefly of myelocytes, for the most part neutrophile; polymorphonuclear neutrophiles with a variable admixture of large

lymphocytes were also present, and the marrow contained also eosinophile cells. The spleen was little altered, while the lymphatic glands were normal, and contained no myelocytes. The authors considered that the finding in these tumours of myelocytes, which are never found in lymphosarcoma, afforded strong evidence for regarding chloroma as allied not so much to lymphosarcoma as to leukæmia, from which, however, it differed in its peculiar localisation and greater aggressiveness.

Sternberg (1905) found in his case 80–100,000 white cells in the blood per cubic millimetre, 69·3 per cent. being large uninucleated cells, 85 per cent. of which had neutrophile granules in the fairly broad band of protoplasm round the nucleus: polymorphonuclear cells, 12·8 per cent.; typical lymphocytes, 17·8 per cent.; very scanty eosinophiles. The growths consisted chiefly of cells with neutrophile granules in the protoplasm corresponding to neutrophile myelocytes, although perhaps a little smaller; there were a smaller number of polymorphonuclear cells and genuine lymphocytes, some cells having neutrophile granules and conforming to the type of Ehrlich's pseudo-lymphocytes. Sternberg considered that chloroma was to be regarded as an atypical growth of the lymphatic apparatus, in most cases closely allied to lymphosarcoma, but in some cases the result of an analogous growth of myeloid tissue. He proposed, therefore, to differentiate two forms of chloroma, an atypical lymphoid tissue growth approximating to lymphosarcoma, and an analogous atypical myeloid tissue growth.

Dock and Warthin (1904), in the case of a man, *æt.* 45, found that 79·6–82·6 per cent. of all the leucocytes resembled closely the undifferentiated lymphocytes of the bone marrow, and classed them as marrow lymphocytes; there were no actual granules in the protoplasm. In the infiltrations a large proportion of the cells were granular, the majority containing eosinophile, a small proportion neutrophile, and a still smaller proportion distinctly basophile, granules in

the protoplasm; the marrow contained cells of the large lymphocyte type, the majority having eosinophile granules; small lymphocytes and polymorphonuclear leucocytes were scanty. Transition forms were also seen, which afforded strong evidence of the development of the cell of the myelocyte, from that of the large lymphocyte, type. The authors considered that chloroma was due to a tumour-like hyperplasia of the parent cells of the large lymphocytes and their descendants, and that these cells might in different cases reach a different degree of development, so as to result in the production in some cases of a lymphocytic, in others of a neutrophile or eosinophile myelocytic, type of tumour. The disease was held to arise primarily in the red marrow, the periosteum being secondarily involved, as could be anatomically demonstrated in one of their cases; it was to be regarded as a more malignant form of leukæmia, the malignancy being greater in the large lymphocytic and atypical forms than in the more highly differentiated myelocytic growths.

Pope and Reynolds, in a case reported in 1907, found 32 per cent. of myelocytes in the blood, and numerous coarsely granular eosinophile cells in the green lymphoid tissue infiltrating the sternum; and in the same year Benjamin and Schule described a case of chloroma with varying leucocytosis, in which myelocytes, typical and atypical, constituted 50 per cent. of the white cells of the blood, while the tumours were composed of granular mononuclear cells.

Treadgold has recently (1908) investigated the subject, and has come to the conclusion that there is reason to suppose that the vast majority of the cells met with in chloroma are abnormal forms of myelocytes and myeloblasts, and that probably by suitable methods some granular cells could have been demonstrated in smears from the infiltrations in every case. The tumour arises in the red marrow of bone. Perhaps in some cases all the undifferentiated marrow cells are affected, yet myeloblasts always form the

majority. In Treadgold's two cases there was reason to suspect that the mononuclear cells seen in large numbers in the blood were abnormal or degenerated myelocytes. He considers that the disease differs from acute leukæmia in the greater prominence of infiltration of the walls of the blood-vessels, greater eroding power of the cells, greater frequency of metastasis, and larger size and greater protoplasm content of the cells.

Finally, in two atypical cases of chloroma, in which periosteal infiltrations were absent, and a green coloration was demonstrable in only a few of the enlarged lymphatic glands, Lehndorff found in the enlarged spleen and glands great numbers of myelocytes and myeloblasts, associated with similar cells in the bone marrow. In the first case, an aleukæmic stage of the blood was followed by an increase of leucocytes from 5,100 to 85,000 per cubic millimetre, while, in the second case, the *post-mortem* findings justified the supposition that the large mononuclear cells, which during life constituted 95 per cent. of the white cells of the blood, and which reached a total of 112,765 per cubic millimetre, were of the nature of myeloblasts. These cases are of exceptional interest, on the one hand, on account of their close clinical resemblance to leukæmia, and, on the other, as affording corroboration of the views advanced by Dock and Warthin, and advocated by Treadgold.

The blood changes most commonly described have consisted in anæmia with increased percentage of lymphocytes, and usually with leucocytosis. According to Rosenblath and Weinberger, the blood changes can set in quite suddenly before death, and Klein and Steinhaus note that towards the end a well-marked leucocytosis frequently develops. Recently, several cases have been reported in which myelocytes were present in large numbers in the blood. Most of these have already been referred to, while in another case Buckmaster found that the majority of the white cells were myelocytes, with minute eosinophile or neutrophile granules. In Dunlop's case the blood contained

5 per cent. myelocytes and 5 per cent. transitional forms, resembling myelocytes, with 73 per cent. lymphocytes, chiefly large. The identification with myeloblasts of the large mononuclear cells present in great numbers in the blood in Lehndorff's second case is suggestive that in some of the previously recorded cases the large cells of lymphocytic type, which constituted a high percentage of the white cells of the blood, may in reality have been of this character.

In view of the above observations, it is clear that, although the evidence on which conclusions can be formed as to the nature of chloromatous infiltrations must be regarded as at present somewhat insufficient and conflicting, yet *in some cases*, at any rate, amongst which is to be included the case here reported, *cells which are normally almost confined to the bone marrow, and which have an important relation to the white cells of the blood, can be shown to form the most prominent constituents of the infiltrations*, a fact which suggests that *such cases, at any rate, must be regarded as examples of a disease arising primarily in the myelogenous component of the hæmatopoietic system*, while the increasing frequency with which in recent times, with improved methods of fixation and staining, such examples have been met with, affords support to the views of those who would attribute to all cases a similar origin.

Of recent years, evidence has accumulated as to the close relationship between chloroma and leukæmia (*cf.* Lehndorff, Frith, and Ledingham), so that some authors, *e.g.*, Naegeli and Fabian, have come to regard chloroma as a species of leukæmia. Sternberg, on the other hand, in view of the aggressive character of the infiltrations, coupled with their incidence in tissues, *e.g.*, periosteum and serous membranes, where rests of lympho-hæmatopoietic tissue cannot be postulated, regards chloroma as a form of sarcoma, distinguishing a chloroleukosarcoma and a chloromyelosarcoma. Pappenheim recognises both a hyperplastic chloromatosis and a chlorosarcoma, between which are to be found all histomorphological intermediate forms. In our case, both the clinical

features and the histological characters of the infiltrations, more especially that in the ovary, were such as to justify a diagnosis of sarcomatosis. The striking predilection of the disease for the bones of the skull and their periosteum is not easy to explain. It seems not improbable that the diseased condition of the middle ear, which has been so frequently recorded in these cases, may here have some causal connection, the chloromatous process taking its origin in the diseased petrous bone, and extending thence to the neighbouring bones of the skull.

There has been much discussion as to the source of the pigment in chloroma, and the point is still unsettled. Balfour believed that it was due to some pigment allied to bile, Dittrich attributed it to putrefaction. Virchow was of opinion that it was diffused in the blood without granular or crystalline deposits. Hüber considered the colour to be due to minute refractile particles in and between the cells, and this opinion was shared by Virchow, Dressler, and Chiari. Dock found abundant highly refractile granules in fresh frozen sections, which disappeared later when the colour of the tumours had faded; similar granules in the renal epithelium were, however, present after the prolonged action of alcohol. Shennan found clusters of similar granules between the cells in Dunlop's case. He believed the granules to be of fatty nature, while Hüber considered them allied to, if not actually, fat; Von Recklinghausen failed, however, to obtain positive results with osmic acid. Reynolds considered that the colouring substance was of the nature of a fatty acid combined with iron, and had very strong reducing power. Trevithick found that the colour was restored by hydrogen peroxide, and Dunlop that it was partially restored by reducing agents. Behring and Wickerkiewicz found in the tumours an unusually high percentage of chlorine. In the case reported here highly refracting greenish yellow granules could be seen in many of the characteristic tumour cells, and also free amongst the cells, their presence and arrangement being possibly due to a degeneration and subsequent

dissolution of the cells. No reaction for free iron could be obtained.

Apart from the affections of the bones, lymphatic glands, spleen, periosteum, and serous membranes, the growth has been found involving almost all the organs and tissues of the body, including the gums, palate, larynx, skin and conjunctiva. The nervous system is, however, very seldom involved, except by pressure, apparently only one instance (brachial plexus) of invasion being reported. The affections of the special senses are interesting. Pfeiffer, in an analysis of 42 cases, found painful exophthalmos with subsequent optic atrophy in 31; optic neuritis and retinal hæmorrhages are also met with. Ear discharge and affection of hearing were found by Pfeiffer 25 times, and in Körner's case the symptoms were such as to lead to incision of both tympanic membranes and a subsequent mastoid operation. Deafness may be produced by disease in the temporal bone, or pressure on the auditory nerve, while disturbance of equilibrium from invasion of the semicircular canals has been described by Körner, Dunlop, Cirincione, and Weinberger. Invasion of the nose may lead to fatal epistaxis (Risel). Green yellow urine has been described by Waldstein and Pfeiffer. Bence-Jones albumose was present in Weinberger's case; in both Rosenblath's cases it was absent.

In the present case the diagnosis of chloroma was not made during life, and both on this account and also in respect of the full description of the case, it is much to be regretted that no blood examination was made. The great proptosis, said to be of rapid development, with distension of the temporal veins, associated with the patient's weak and emaciated condition, seemed to point not improbably to a thrombosis of the cavernous sinus of either marasmic or tuberculous nature, the latter origin being favoured by the patient's previous history, the distended abdomen, and the subsequent development of physical signs at the left lung apex and of middle ear disease. A thrombosis of acute infective origin could be excluded from the diagnosis by

the absence of severe head symptoms and the character of the temperature. Local inflammatory conditions, intra-orbital hæmorrhage in the course of scurvy rickets, and aneurism, could also be eliminated. In the later stages the possibility of the condition being sarcoma was discussed, and in such cases the frequency of the development of orbital metastases in association with suprarenal sarcoma should always be borne in mind. The development of a pulsating swelling in the left occipital region, together with a bruit heard both here and behind the angle of the right jaw, was a puzzling feature. The *post-mortem* examination showed the condition to be due in all probability to a communication, through a very large mastoid emissary vein, of the blood in the plexus of veins which is normally present in the occipital region, with that in the left lateral sinus, the abnormal condition of the sinus walls being responsible for the bruit. The clinical picture was further complicated by the development, in association with high temperature, of a swelling behind the left ear presenting the typical features of a mastoid abscess, and containing what was apparently green pus. It seems probable that the swelling was, in fact, of infective origin, the appearance of its contents being influenced by the character of the blood, and the chloromatous disease of the middle ear and its neighbourhood.

That tarsorrhaphy should have been successful in arresting the progress of the corneal ulceration, in spite of the great difficulty experienced in obtaining approximation and union of the lids, is perhaps worthy of note.

In conclusion, I have to express my thanks to Mr. Arnold Lawson for permission to make use of the clinical notes of the case, to Mr. George Coats for the use of many microscopic sections and the *post-mortem* notes, and to Mr. L. S. Dudgeon for his advice and help in the interpretation of the cytology of the infiltration.

Much of the bibliography of the subject has been collected by Hall, Hebb, and Bernstein (Chloroma. Proc. Roy. Soc. Med., vol. ii, No. 5, 1909).

The following references may be added:—

Benjamin. Jahrb. f. Kinderh., vol. lxv, 1907 (literature).
Bernheimer. Bericht der Heidelb. Ophth. Gesellsch., 1889.
Borst. Die Lehre von der Geschwülsten.
Bramwell. Clinical Studies of Chloroma. Edinb., October, 1904.
Butler. B. M. J., 1907, vol. i.
Fabian. Beit. z. path. Anat. u. z. allg. Path., 1908, vol. xliii.
Firth and Ledingham. Proc. Roy. Soc. Med., vol. iv, No. 2 (recent literature).
Hichens. B. M. J., 1903.
Hillier. Trans. Path. Soc. Lond., 1855.
Lehmann. St. Petersb. Med. Woch., 1906, vol. xxi, p. 411.
Pappenheim. Folia Hæmatol. Leipzig, 1909, vol. vii, p. 449.
Steinhaus. Arch. de Med. exp. et d'Anat., 1909, vol. xxxi, p. 64.
Sternberg. Chlorom. Ergeb. d. allg. Path., 1905, vol. ix.
Sternberg. Münch. Med. Woch., 1902, No. 3.
Treadgold. Quart. Journ. Med., 1910.
Ziegler. Lehrbuch d. allg. Path., 1904.

A NOTE ON CERTAIN PECULIAR PIGMENTARY MARKINGS IN THE CORNEA.

By A. C. Hudson.

[With Plate XIV, Fig. 3.]

The appearances to be described were met with, for the most part, in the routine examination, previous to operation, of in-patients at the Royal London Ophthalmic Hospital during the years 1907 and 1908. Cases have also been met with subsequently amongst other patients.

The appearance met with most commonly was that of a linear, horizontally disposed, brown mark situated about at the junction of the middle and lower third of the cornea, to the more central part of which it was confined, so that the extremities in no case extended to the limbus. The line was in all cases of extreme tenuity, being seldom visible except to the most careful examination under the corneal microscope. In some cases it exhibited a fairly abrupt definition, presenting the appearance of a pigmented fissure; but, in the majority of examples, the pigmentation faded imperceptibly into the surrounding cornea. The depth of its situation could not be satisfactorily gauged, but the impression was received that this was but a short distance beneath the surface of the cornea. The overlying epithelium was in all cases smooth and bright. Although in the great majority of cases the marking was horizontally disposed, it occasionally showed an oblique orientation. In all cases in which this type of marking was met with, the cornea was apparently in other respects normal, and in no case could any evidence of previous inflammation be elicited.

The line was met with in 13 cases of senile cataract, the youngest patient being 54 and the average age 62·5 years. Eight of these patients were females and five males. The

line was present in both eyes in eight of these cases, in one of which, a woman aged 55 years, one eye was, apart from the presence of the line, normal; while in one of the remaining seven cases, in all of which the lens opacities were bilateral, the line was more evident in the eye with the less advanced lens changes. In the other five cases of senile cataract the line was noted in one eye only. In all of these five cases the lens opacities were bilateral, and in two of them the eye in which the line was seen was the one with the less advanced lens changes.

The line was also met with in the eye of a female patient aged 38, in association with unilateral cataract; the iris was of blue-grey hue, and the changes in the lens were in all probability secondary to an affection of the ciliary body.

Other cases in which the line was seen were a female patient, aged 55, who had recently had an operation on both eyes for acute glaucoma, in whom the line was seen only in the eye which had recovered with full vision; a male patient, aged 64, the subject of unilateral absolute glaucoma, in whom the line was present in the affected eye only; an elderly man whose lens had recently been completely dislocated backwards, the line being confined to the affected eye, which, apart from the displacement of the lens, appeared healthy; and a man, aged 25 years, the subject of concomitant convergent squint. In the last-mentioned case the line was bilateral and of greyish-brown hue, intensely fine, and typically disposed; it was visible both by oblique and direct ophthalmoscopic examination. The vision of the two eyes with correction of the refraction was respectively 6/6 and 6/60. The patient was a somewhat ill-nourished individual, but no history of previous inflammatory disease, or exposure of the eyes to adverse conditions, could be elicited.

Up to the present date no microscopical examination of the condition has been made. The absence of all history of previous inflammation and of demonstrable blood-vessels in the cornea seems to negative the probability of a hæmatogenous origin for the brown markings. The situation

of the line appears to point to the influence of exposure, and perhaps also to that of the lid movements, as important factors in its development; and this, coupled with the peculiar coloration, resembling to some extent that met with in cases of hyaline degeneration in the cornea, more especially as it is met with in the substance of old scars, is suggestive that the appearance may be the expression of a minimal degree of such degeneration occurring as a primary change in a part of the cornea where the lid movements would be least efficacious in obviating a stagnation of fluids in the tissues, a condition which would be favoured by any enfeeblement of the vascular circulation at the corneal margin, such as is not unlikely to occur in old age. Should this explanation be proved to be correct, it would involve the recognition of primary hyaline degeneration in the cornea as a much commoner event than has generally been supposed.

A somewhat similar appearance was observed in a case of conical cornea of fairly pronounced degree in a female, aged 43, who was admitted to the Royal London Ophthalmic Hospital under Mr. Lang in 1908 (Reg. No. 1768). In this case a brown line could be seen, under high magnification, forming an almost complete circle in the cornea at about the junction of the peripheral two- with the central three-fifths, but having its centre of curvature slightly below that of the cornea (Plate XIV, Fig. 3). The borders of the line were very ill-defined, the peripheral more so than the central; and it could be distinguished as an ill-defined shadow against the fundus reflex. The line was more distinct in its lower than in its upper part, where a short break in the circle occurred. At the outer and lower part of the cornea were several exceedingly delicate, cobweb-like, perfectly straight linear markings, which passed inwards in a radial direction from the periphery of the cornea on a plane anterior to the brown ring. These lines could not be distinguished with the ophthalmoscope, and both on this account and in view of their geometrical conformation, were unlike blood-vessels. Splits in Descemet's membrane and opacities in the neighbour-

hood of the summit of the conus were not present. The cornea of the fellow eye, in which the conicity was of very slight degree, presented no abnormal markings.

The patient was thin and anæmic and of neurotic disposition. She stated that she was never well; but no evidence of organic disease was found.

Since observing this case the writer has met with similar appearances in other cases of conical cornea, in one case a ring-like brown line being seen, while in two others the markings have been of more limited extent.

The only references to similar observations in association with conical cornea which the writer has been able to find are those of Fleischer (Münchener Med. Wochensch., 1906, p. 625), who, in a case of bilateral conical cornea with opacities and fine blood-vessels in each cornea, observed in each eye after enucleation a brown ring, situated about half-way between the centre and the periphery of the cornea. The pigmentation was demonstrated to be due to an iron-containing pigment, probably hæmosiderin, confined to the corneal epithelium, the deepest layer of which was most extensively affected. The condition was attributed to the presence of blood pigment which had gained access to the corneal tissues from the minute blood-vessels present there. If this explanation be correct, the limitation of the pigment to the epithelium is remarkable; nor does it appear to have presented the granular appearance usually met with in cases of blood-staining of the cornea. The same author met with a similar condition in the living eye in a case of conical cornea, with opacities and new vessel formation.

There can be little doubt that the appearances which we have noted are essentially the same as those met with by Fleischer, and must therefore, on the strength of his findings, be regarded as the result of hæmatogenous pigmentation. On this assumption, it seems probable that the fine grey lines noted in the case depicted in Plate XIV were, in spite of their peculiar conformation, in reality

minute blood-vessels. In this case the brown pigmentation, inasmuch as it was situated on a plane posterior to the grey lines, must have involved tissues lying more deeply than the epithelium, a point in which the case differs from that of Fleischer. It seems likely that the peculiar distribution of the pigmentation is in some way dependent upon an abnormality, either in structure or in curvature, of that portion of the cornea constituting the conus, the more abrupt margin of pigmented area corresponding with the base of the cone.

Fig. 1.

Fig. 2.

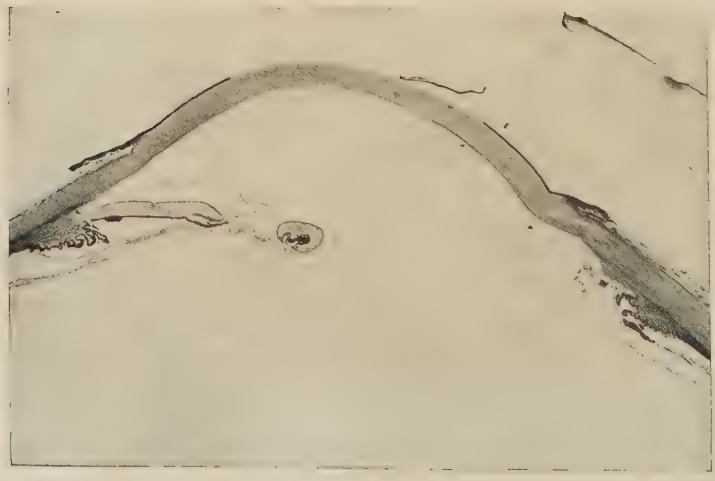

Fig. 3.

INJURY TO THE VITREOUS BODY AS A FACTOR IN THE PRODUCTION OF SECONDARY GLAUCOMA.

By A. C. Hudson.

[With Plate XV.]

The manner in which adhesion of the vitreous to a scar situated in front of the anterior excretory channels of the eye may be responsible for an increase in intra-ocular tension has long been recognised, and is capable of an explanation which is on the whole satisfactory. This class of case will, therefore, not be dealt with in this communication, the object of which is an enquiry into the part played by injury to the vitreous in certain conditions in which its influence is not so generally recognised; namely, glaucoma consequent on subluxation and on backward dislocation of the lens, and glaucoma following discission of after cataract. The treatment of these conditions will also be discussed.

For the purposes of this enquiry a clear conception of the normal gross anatomy of the vitreous body is essential. In globes hardened in Zenker's fluid and divided antero-posteriorly the vitreous body is seen to consist of a ground-work of fibrils radiating inwards from an attachment in the region of the ora serrata. The fibrils are composed peripherally of numerous lamellæ, the plane of whose origin coincides with the coronal plane of the eyeball, while the planes of the various radiating lamellæ present a varying degree of concentricity with the antero-posterior curvature of the globe. The lamellæ are united by delicate fibrils and are most consistent in the equatorial region, while in the most anterior part of the vitreous they form an interlacement behind the lens; in the more central parts of the vitreous the fibrils are more irregularly disposed. Anteriorly the most peripheral lamella may be traced from the most anterior part of the vitreous attachment forwards and inwards as an

anterior hyaloid membrane behind the zonula and the lens, with whose posterior capsule it is in loose connection, to the corresponding point of the vitreous attachment of the opposite side; while posteriorly the most peripheral lamella passes backwards as a posterior hyaloid membrane to obtain an attachment at the margin of the optic disc. The spaces of the fibrillar structure thus constituted are filled with a fluid of a composition almost identical with that of the aqueous humour.

Glaucoma Consequent on Complete Backward Dislocation of the Lens.

The pathological anatomy of an eye enucleated on account of glaucoma consequent on dislocation of the lens into the vitreous chamber has been described by Lawford and by Straub. In each case the angle of the anterior chamber was open; in Lawford's case, however, in which the dislocation had existed for 12 years, while acute symptoms were of recent onset, there was an aggregation of cells in the meshes of the ligamentum pectinatum and about Schlemm's canal, which the author suggested might not unreasonably be expected to retard the outflow in this situation. The anterior chamber was filled by a coagulated, soft, semi-transparent effusion, but there was no histological evidence of inflammation of the iris. The vitreous over the lens showed no naked eye change. Straub's case was complicated by the presence within the eye, from the date of the original accident 10 years previously, of a fragment of steel. Straub could find no satisfactory connection between the lens dislocation and the raised tension. In neither case was any evidence adduced that an abnormal relation of the vitreous had played any *rôle* in the production of the glaucoma. That such, however, may be the case in some instances of glaucoma associated with total lens dislocation seems to be evidenced by the following observations.

Case 1.—Mary S., *æt.* 67, was admitted to the R.L.O.H., under Mr. Marshall, on September 25th, 1906.

The right eye had been defective since a blow received seven

and a-half years previously, and had been red and painful 10 months, and again three weeks before admission to hospital. The second attack was associated with vomiting.

On examination there was ciliary injection of the right eye with vesicular keratitis. There were no post-corneal deposits, but cholestearin crystals could be seen suspended in a jelly-like fluid immediately behind the cornea. The anterior chamber was deep. The tension was + 2, and the vision p.l.

The eye was excised, hardened in formalin and divided sagitally (Reg. No. 7340).

Macroscopical Appearances.

The anterior chamber is deep and the angles open. The lens lies free in the vitreous. Retina and choroid are *in situ*. The optic disc is slightly cupped.

Microscopical Appearances.

The angle of the anterior chamber is open and the spaces of the ligamentum pectinatum are well formed, but are extensively choked by large swollen cells with small dark eccentric nuclei, which are also present in the crypts, and in small numbers in the tissues, of the iris, and in the vitreous. The iris and ciliary body are somewhat atrophic, but there is no evidence of inflammation, except for the presence of a few mononuclear cells in their tissues. The zonula and the anterior hyaloid membrane are absent. The choroid is atrophic. The inner layers of the retina and the optic nerve are very atrophic.

The anatomical changes in this case presented a very close resemblance to those found in Lawford's case, sections from which the writer has had the opportunity of examining. In each case the spaces of the ligamentum pectinatum contained large numbers of swollen cells with eccentric nucleus such as are not uncommonly met with in the vitreous in chronic inflammatory conditions, and in each case the anterior chamber contained a viscid material. The writer is inclined to regard this material in his case as altered vitreous rather than inflammatory exudate, on the one hand on account of its clinical appearances, and on the other in view of the acute

character of the symptoms, which would accord rather with a condition of glaucoma set up by the passage forwards into the anterior chamber of vitreous, and the consequent interference with fluid outflow at the angle of the chamber, than with a similar condition due solely to cellular obstruction, probably of long standing.

CASE 2.—Clara R., *æt.* 43, was admitted to the R.L.O.H., under Mr. Lang, on December 13th, 1909.

The patient had been struck in the right eye whilst chopping wood by a large fragment nine days previously. There had been much pain in the eye since the accident.

On examination the right pupil was found to be wide and fixed. The lens was dislocated into the lower and outer part of the vitreous chamber. The tension was + 1.

Paracentesis was performed two days after admission to hospital, cyclodialysis eight days later, and paracentesis again three days later. As, however, the eye continued very hard and painful it was excised on January 6th, 1910.

The eye was hardened in Zenker's fluid, and divided anteroposteriorly in a direction downwards and inwards (Reg. No. 8015).

Macroscopical Appearances.

The lens is dislocated downwards and outwards and lies on the ciliary processes. The iris is markedly bombé, and the angle of the anterior chamber is occluded everywhere by the apposition of its root to the tissues forming the anterior boundary of the angle. The vitreous is of healthy consistence.

Microscopical Appearances.

The cornea is normal except for a slight amount of œdema of its tissues and some desquamation of its epithelium.

The iris is markedly bombé and the angle of the anterior chamber is everywhere occluded by apposition of its base to the ligamentum pectinatum and Descemet's membrane. The endothelium of Descemet's membrane is healthy. The tissues of the ligamentum pectinatum are compressed, somewhat more so above than below; but the individual trabeculæ are recognisable. The channels of Schlemm's canal are patent and contain blood,

while the surrounding tissue is somewhat hypercellular and holds some pigment masses in its meshes. The iris tissue is free from signs of inflammation; its peripheral portion is compressed. The ciliary processes are somewhat compressed, and in all sections are separated by a considerable interval from the root of the iris.

The vitreous passes through the pupil into the anterior chamber, in many sections in the form of a ballooned membrane which contains in its posterior part, and on its posterior surface, masses of pigment, and red blood corpuscles (Plate XV, Fig. 1). This hernia-like protrusion is in contact with both margins of the pupil, and above (on the right of the figure) it is obviously adherent, the adhesion being evidenced by ectropion of the pigment layers of the iris, and a hummock on its anterior surface, clearly produced by the forward traction of adherent vitreous. Below an adhesion is indicated by the intimate relation of the structures concerned, and by ectropion of the pigment layers. In other sections a voluminous mass of fibrillated vitreous overhangs the lower pupillary margin into the anterior chamber, reaching almost as far as the false angle; while a delicate, somewhat granular string passes forwards from the upper vitreous origin to the upper pupillary margin, to become continuous with a similar material on the anterior surface of the iris. This material appears to be degenerate vitreous, and is continuous with a dense mass of similar appearance which occupies the upper false angle of the anterior chamber; small masses are also present in the lower false angle. Both above and below there is ectropion of the uvea. In peripheral sections of the lower and outer part of the anterior chamber the hernia-like vitreous protrusion is seen almost to fill the chamber.

The posterior chamber, bounded by the vitreous as it passes from its origin to the pupillary margin, is considerably distended. The vitreous at its origin is in places degenerate, and contains a few red blood corpuscles, but otherwise it shows no pronounced abnormality.

The fibres of the suspensory ligament of the lens are not visible further forwards than the level of the pars plana of the ciliary body.

The retina, choroid and sclera are normal in appearance.

In this case the sequence of events leading to the anatomical conditions found may not improbably have been as follows: A violent dislocation of the lens has resulted in an extensive rupture of the diaphragm constituted by the suspensory ligament of the lens and the anterior hyaloid membrane, which normally supports the vitreous anteriorly, together with considerable laceration of the anterior consistent portion of the latter, which has thus been enabled to pass forwards into apposition to the pupil, forming an irregularly felted membrane across it. It is easy to conceive that such a forward movement of the anterior part of the vitreous might in itself be responsible for a forward movement of the iris. Such a supposition would, however, not suffice to account for the bombé formation of the iris and the condition of the posterior chamber, together with the redundant character of the vitreous protrusion, features which seem to point to a somewhat more complicated mechanism such as the following: As the result of apposition of the vitreous diaphragm to the pupillary margin some obstruction to the free passage of aqueous from the posterior to the anterior chamber has occurred, the effect of which has been twofold, in the first place an over-distension of the posterior chamber, giving rise to the condition of bombé iris, and in the second place, as a result of the passage of fluid from the posterior chamber forwards to the anterior chamber by an indirect route through the vitreous, a ballooning forwards of the vitreous diaphragm in the pupil, so that it has come into contact with, and in places at any rate has become adherent to, the anterior surface of the pupillary portion of the iris, a condition likely to accentuate the obstruction to direct passage of aqueous from posterior to anterior chamber. It is conceivable that this ballooning process may have been accentuated by an increased osmotic pressure within the vitreous dependent on the presence there of blood constituents; while both it and the distension of the posterior chamber would be favoured by evacuation of the anterior chamber by operation. As the result of these

factors the iris has become bowed forward to such an extent that its root has become applied to the tissues forming the anterior boundary of the angle of the anterior chamber, and in this manner a condition of acute glaucoma has been established.

Case 3.—I am indebted to Major Elliot, I.M.S., for this specimen.

T. P. M., male, *æt.* 58. Couching operation for cataract performed by a native Indian practitioner four months before excision. The sight remained good for a fortnight after the operation, when there was a sudden onset of pain in the eye, with progressive failure of vision. At the date of excision there was well marked circumcorneal injection with haze of cornea and tension + 1. The anterior chamber was practically absent, the pupil dilated and oval. The lens could be seen in the lower and outer part of the vitreous. V. = h.m.

The globe was fixed in formalin solution, and was divided vertically (Reg. No. O.P. 1000.)

Macroscopical Appearances.

The lens rests loosely behind the ciliary processes, which are separated by a considerable angular interval from the iris, so that nowhere apparently does the lens make pressure either directly or indirectly on the iris. The iris is markedly bombé, and is very extensively adherent to the corneo-sclera. The vitreous is for the most part clear and fluid, but around the lens and behind the ciliary body and iris is vitreous of somewhat stringy consistence, which passes into the pupil, where it is adherent apparently all round to the pupillary margin. It projects forwards slightly into the anterior chamber, to the upper angle of which a strand can be traced. There is a commencing equatorial staphyloma above and below.

Microscopical Appearances.

The corneal epithelium is loosened in places. The iris is somewhat atrophic, and is adherent by its peripheral two-thirds to the tissues of the ligamentum pectinatum and posterior surface of the cornea (Plate XV, Fig. 2). The trabeculæ of the

ligamentum pectinatum are much compressed, the individual fibres being indistinguishable. The situation of Schlemm's canal is occupied by a hypercellular tissue containing numerous masses of pigment. The pupillary third of the iris is markedly bombé, and the backwards directed pupillary border is adherent to irregular strands of vitreous which pass forwards from the region of the ora serrata. In some sections vitreous is seen passing between the margins of the pupil as a membrane with a convexity forwards. The fibres of the suspensory ligament are not seen further forward than the level of about the middle of the ciliary processes. The ciliary body is very atrophic. The retinal and choroidal vessels are healthy. The optic disc is deeply cupped.

The anatomical findings in this case point to a condition of glaucoma secondary to over-distension of the posterior chamber and consequent bombé iris of origin essentially similar to that found in the preceding case.

In this connection it may be of interest to note that Maynard* in an examination of 63 cases in which a couching operation for cataract had been performed found 10 cases of glaucoma. One case had probably been the subject of glaucoma before operation. Elliot† found the complication in 8 per cent. of 125 cases treated by couching.

Case 4.—Female, *æt.* 60 (Spec. 1, *a*, 14, R.L.O.H. Museum). The eye was struck by a piece of wood three weeks before enucleation, and had been very painful since the injury.

Macroscopical Appearances (*no Microscopical Sections*).

The lens lies in the lower part of the vitreous just behind the ciliary body. There is a hernia of the vitreous into the pupil, and adhesion of the iris almost as far forwards as its pupillary border to the back of the cornea. The retina is *in situ*, and the optic disc is slightly cupped.

The anatomical changes in this case point to a forward movement of the anterior part of the vitreous, consequent

* Ophth. Rev., 1903, p. 91.
† Ophthalmoscope, 1906, p. 193.

on a loss of anterior support, as the main factor in the causation of the apposition of the iris to the cornea and the resultant glaucoma. The situation of the lens and the very extensive character of the iris adhesion of rapid formation may be held to preclude the probability of the changes being due on the one hand to mechanical pressure of the lens on the ciliary body and iris, or on the other hand to the results of inflammation.

Case 5.—I have to thank Mr. Lawford for this specimen.

S. L., male, *æt.* 44. The right eye had been injured three years and four months before enucleation by a blow from a "diabolo" causing iridodialysis and backward dislocation of the lens. There had been a gradual development of glaucoma, and at the date of excision (March 13th, 1911) perception of light had been lost and the tension was + 3. The deep parts could not be seen.

The eye was hardened in Zenker's fluid and divided antero-posteriorly in a direction downwards and outwards (Reg. No. O.P. 1113).

Macroscopical Appearances.

The lens is dislocated into the lower part of the vitreous chamber, lying just behind the ciliary body. The iris has become separated at its root in the lower and outer half of its circumference, the separated portion occupying a position which corresponds approximately with a central meridian of the cornea. It is horseshoe-shaped in section, its posterior surface showing a concavity which is directed upwards, inwards, and slightly backwards, while its anterior surface is directed downwards and outwards. The vitreous is considerably disorganised and passes forwards so as to completely occupy the pupil in the form of a membrane adherent to its margins. In the area of the false pupil formed by the iridodialysis strands of vitreous pass forwards on one side to become attached in the region of the ligamentum pectinatum over the whole area involved by the iridodialysis, and on the other side over the convex border of the separated iris to become continuous with a delicate semi-transparent membrane which passes upwards and inwards over the iris and pupil. At the level of the section this membrane can be traced to an attachment in the region of the ligamentum

pectinatum, and is seen to be separated everywhere by a definite space from the upper and inner (non-detached) portion of the iris. In the upper segment of the eye this space can be demonstrated for a distance of about 3 millimetres, when it apparently becomes obliterated by union of the membrane with the surface of the iris. The relations of the membrane in the lower half of the eye will be detailed in the description of the microscopical appearances. The lower part of the angle of the anterior chamber is occupied by a dense granular material. The tunics are *in situ* and the optic disc is not cupped.

Microscopical Appearances in Serial Section of the Lower and Inner Half of the Globe (Plate XV, Fig. 3).

The corneal epithelium is œdematous and extensively desquamated. The anterior chamber is deep. Both above and below a partial rupture of the ligamentum pectinatum has occurred, and has resulted in a slipping back of the inner part of the ciliary body. Above, the iris has been carried back with the ciliary body; in no section is it found to obstruct the angle of the anterior chamber. Below, the rupture is more extensive, and here the iris has been completely torn away from its origin. At the site of the rupture of the ligament, and overlying the intact portion, on this side, is a mass of hyaline-like laminated material, containing oval nuclei and flattened pigment-bearing cells in its interstices. Strands of vitreous pass forwards to become connected with this mass, and from it a process of similar formation to the main mass juts inwards for a short distance into the false pupil. The fibres of the ligamentum pectinatum are sclerosed and somewhat compressed. Schlemm's canal is well formed. At the opposite margin of the false pupil strands of vitreous pass forwards on to the convex border of the separated iris, where they become continuous with a thick hyaline membrane clothed on each surface by endothelium, which passes across the true pupil and then in front of, but not in contact with, the intact iris to unite with the ligamentum pectinatum of this side at about its middle point. At the point of union the single membrane appears to divide into two thinner ones, which pass backwards and forwards clothing the surface of the ligament. As this membrane is traced down-

wards in consecutive sections it is found to become thinner in section, while its extensions on the surface of the ligament are also more delicate in texture. At a rather lower level is seen an aperture in the membrane just within its point of termination, and slightly further down it fails to reach the ligamentum pectinatum, terminating by union with the surface of the unseparated iris. At a slightly lower level it is again found as a well formed membrane, which not only reaches the ligamentum pectinatum, but also extends for a short distance across the false pupil towards the stunted membrane jutting inwards from the opposite side. These two membranes are subsequently found to become continuous one with another, so that sections through the lowest part of the angle of the anterior chamber show a single membrane of very considerable thickness which passes continuously from the hypertrophied mass on the side of the iridodialysis to terminate in an elaborate open-work hyaline reticulum which completely occupies the angle of the opposite side. The true pupil is everywhere traversed by delicate membranes consisting of vitreous upon which a few nucleated cells are seen. The iris on each side is slightly atrophic but shows no evidence of inflammation.

The ciliary body is also free from signs of inflammation. The inner portion of the ciliary muscle on each side is somewhat atrophic.

The retina is *in situ*. The nerve fibre and ganglion cell layers are atrophic and œdematous, and the supporting fibres are hypertrophied. The walls of some of the veins are degenerate and infiltrated with mononuclear cells.

The choroid is thinned, chiefly as the result of compression.

The optic disc is not cupped. The optic nerve is slightly atrophic.

The special interest of this case lies in the fact that the slowly developing glaucoma was probably to be attributed to the formation of a hyaline membrane lying more or less free in the anterior chamber and partially clothing the inner aspect of the ligamentum pectinatum. The character and relations of this membrane point to an origin from the endothelial cells of the ligamentum pectinatum. That it differs

essentially from the hyaline membranes found on the surface of the iris as the result of inflammatory conditions of long standing: is evidenced by its almost complete dissociation from the iris, by the presence of an endothelial lining on each surface, by its extension into and across the false pupil, and, most of all, by its reticular structure in one part of the angle of the anterior chamber. A more probable explanation of its formation, and one which would accord with its relation to the vitreous, is afforded by the supposition that as the result of severe injury strands of vitreous have passed through the pupil and the false pupil into contact with the injured ligamentum pectinatum, and have afforded a scaffolding for the growth of the endothelial cells found in this situation, and for the subsequent deposition of hyaline-like material similar to that met with in the fibres of the ligamentum pectinatum.

The anatomical findings in the foregoing cases afford evidence that injury to the vitreous body, associated with complete backward dislocation of the lens, may lead to increased intra-ocular tension in more ways than one; firstly, from passage forwards of the vitreous into the anterior chamber, and consequent obstruction of the channels of exit at its angle and the iris crypts: secondly, from direct forward pressure of the vitreous on the iris, and consequent closure of the chamber angle by the iris root; thirdly, from an accentuation of such forward movement of the iris by over-distension of the posterior chamber as the result of ballooning of vitreous through the pupil, and consequent interference with the perfectly free passage of fluid from posterior to anterior chamber; and, fourthly, as the result of vitreous which has passed into the anterior chamber affording a scaffolding for the growth of endothelium of the ligamentum pectinatum and the subsequent deposition of impervious hyaline membranes which obstruct the passage of aqueous to the spaces of the ligamentum pectinatum. The second of these methods of the causation of glaucoma was recognised by Treacher Collins, who, writing in the Museum Catalogue

(1893) of the R.L.O.H., states that "when the lens becomes displaced backwards or laterally, and increased tension results, it is probably due to the relative alteration in position which has taken place between the lens and the vitreous body, directly forcing forwards the root of the iris into contact with the cornea, so closing the angle of the anterior chamber; for in these cases the angle is always found to be closed."

Before leaving this part of the subject, it may be of interest to notice that the sequence of glaucoma on the operation of extraction of the lens in its capsule, which might at first sight be expected to be a comparatively common complication, would appear to be an event of rare occurrence. This is probably to be explained by the fact that the operation does not necessarily involve extensive injury to the zonular diaphragm, owing to the tendency of the line of separation of the lens in its capsule to coincide with the lenticular attachment of the zonular fibres.

Glaucoma Associated with Subluxation of the Lens.

Anatomical descriptions of eyes exhibiting this condition have been published by several authors. Thus Priestley Smith examined an eye which was excised six days after an injury on account of glaucoma following on subluxation of the lens. He found the angle of the anterior chamber closed over an extensive area, and attributed the condition to pressure forwards of the iris on the one side by the lens through the medium of the ciliary processes, and on the other by an advance of the vitreous (without rupture of the hyaloid membrane) as the result of its displacement to the opposite side by the dislocated lens.

Lawford, in two eyes excised respectively 12 months and 24 days after injury causing subluxation of the lens and glaucoma, found the periphery of the iris applied to the cornea. He regarded the condition as due, on the one hand, to pressure forwards of the iris by the lens on the side of

the subluxation, and on the other to the excessive work of excretion thrown on the angle of the opposite side.

In Terson's case of glaucoma following downward subluxation of the lens of eight months' duration, the angle of the anterior chamber was nowhere closed. The vitreous was fluid, and there was a perfectly free passage between the anterior and posterior chambers. There was no evidence of inflammation of iris or ciliary body. Terson attributed the glaucoma to degenerative changes in the retina, secondary to the subluxation of the lens.

Alt has described a case of glaucoma ensuing seven months after an injury causing subluxation of the lens downwards and outwards, and complicated by an iridodialysis and rupture of the ligamentum pectinatum above. At the site of the rupture and in Schlemm's canal was an accumulation of pigment molecules, and a similar material was found in the meshes of the ligamentum pectinatum, and in Schlemm's canal below, where the iris was pressed forwards against the cornea by the dislocated lens. The iris and ciliary body were much infiltrated with round cells. Alt concluded that the condition of Schlemm's canal would readily explain the increased intra-ocular pressure.

In Ischreyt's case glaucoma had followed a slight upward and outward subluxation of the lens produced by a blow received a year previously. The root of the iris was firmly adherent to the sclera, and the spaces of Fontana and Schlemm's canal were unrecognisable. Forward pressure of the iris by the lens was not found, and the author was of opinion that a sudden hypersecretion of fluid might have played some part in the forward displacement of the iris.

From the above *résumé* it is evident that none of the above-mentioned authors attributed any share in the causation of the glaucoma to an abnormal relation of the vitreous, with the exception of Priestley Smith, who advanced the supposition that in his case the obliteration of the angle of the anterior chamber on the side opposite to the subluxation had been produced by a displacement forwards of the vitreous

against the posterior surface of the iris, as a result of the movement of the lens. Treacher Collins, in the passage referred to in dealing with dislocation of the lens into the vitreous, expressed the view that in these cases also glaucoma is probably due to the relative alteration in position which has taken place between the lens and the vitreous body, directly forcing forwards the iris root into contact with the cornea. He gives as an example of this mechanism Specimen iii, *b*, 3, in the R.L.O.H. Museum, an eye which had become blind from glaucoma following a blow received two months before enucleation. In this eye the lens is displaced forwards and a little downwards, exerting a forward pressure on the iris. The iris is pushed forwards into contact with the cornea, and the angle of the anterior chamber is everywhere closed. The vitreous is detached posteriorly, and passes forwards between the upper margin of the lens and the ciliary body, pushing the iris before it. The optic disc is deeply cupped.

That a forward movement of the vitreous of even more extensive character than in the case just referred to is liable to follow a rupture of zonula and anterior hyaloid membrane consequent on subluxation of the lens is evidenced by the fact that it is sometimes possible to discern in clinical examination a hernia of vitreous into the anterior chamber between iris and dislocated lens, and also by the anatomical conditions in the following cases :—

Case 6.—Specimen 1, *a*, 29, R.L.O.H. Museum.

Male, *æt.* 56. Eye struck by a piece of wood one month before date of excision. No perception of light.

The lens is displaced outwards and exerts some forward pressure on the iris. The vitreous is detached posteriorly and passes through the inner part of the pupil across the anterior surface of the lens and towards the opposite angle of the anterior chamber. The iris is adherent at its root to the cornea throughout its circumference; the adhesion is, however, much more extensive at the inner side, where it is pressed forwards by the vitreous as it passes through the pupil, than at the outer

side, where the subluxated lens is responsible for the displacement. The optic disc is deeply cupped.

CASE 7.—Specimen 1, *a*, 6, R.L.O.H. Museum.

The eye received a blow three weeks before the date of excision. There was no perception of light, and the intra-ocular tension was raised.

The lens is displaced laterally, and presses on the ciliary processes. At the opposite side the vitreous passes through the aphakic portion of the pupil on to the anterior surface of the iris. The root of the iris is applied to the corneo-sclera throughout its circumference. The optic disc is cupped.

CASE 8.—Specimen 1, *a*, 7, R.L.O.H. Museum.

Male, *æt.* 6. Eye struck by a stone eight days before enucleation. Intra-ocular tension low.

The lens is displaced outwards and backwards. The vitreous protrudes between it and the iris into the anterior chamber, exerting a forward pressure on the iris. It then passes across the anterior surface of the lens on to the anterior surface of the opposite iris, to which it is apparently firmly united, the appearances suggesting that vitreous tissue has passed into the crypts in the neighbourhood of the circulus iridis minor. The angle of the anterior chamber on the side to which the lens is dislocated is open, and at the opposite side it is prolonged outwards by a rupture into the ciliary body.

It will be noted that in three of the four cases referred to above glaucoma had resulted from obstruction of the angle of the anterior chamber by the root of the iris, as a result of a forward movement of the latter. That the vitreous hernia between iris and dislocated lens had been an important factor in the production of this forward movement of the iris can scarcely be doubted. This seems especially evident in Case 6, where the very extensive character of the adhesion on the side opposite to that to which the lens is displaced could not be satisfactorily explained as the result of an extension of an adhesion originating on the side of the dislocation as the result of direct pressure forwards of the iris by the lens.

Glaucoma Consequent on Discission of Capsular Membrane.

That the operation of discission of capsular membrane may be followed by increase of intra-ocular tension has long been recognised. Thus Bowman, writing in 1865, refers to this complication, noting its relatively greater frequency after simple than after combined extraction. "Probably the iris will be found more or less bulged forwards, showing accumulation of fluid behind it in a space not communicating with the anterior chamber." Bowman attributed the condition to laceration of the more consistent vitreous in the ciliary region, causing it to press thence afterwards through the pupil, causing irritation of the iris by displacement, and consequent heightened tension.

Heymann (1867) met with the condition in association with iritis five years after discission of after-cataract in a case in which a linear extraction without iridectomy had been performed, and attributed it to the shaking of the tremulous membrane.

Von Graefe (1869) believed the complication to be due to swelling of lens remnants, and to tearing and irritation of the ciliary processes. He was of opinion that in most of Bowman's cases an annular posterior synechia existed; as only in association with this condition was a condition of bombé iris met with.

H. Knapp (1894) reported 16 cases of glaucoma following discission of membrane after simple extraction. In all the cases bombé iris was associated with the glaucoma, independently of the presence of posterior synechiæ. Knapp considered that in some cases glaucoma might have been due to the swelling of lens remnants, but that in most cases, as such remnants were not present, the predominating cause was traction on the ciliary processes. In all cases in which iridectomy was performed, vitreous apparently normal in character welled out of the wound, pointing to an increase in volume of the vitreous.

A. Pagenstecher (1895) stated that he had often observed

the complication, and believed it to be sometimes the result of swelling of remains of lens cortex, while in other cases mental excitement before operation favoured the development of glaucoma.

Bayardi (1896) advanced the opinion that the condition was due to an invasion of the anterior chamber, and obstruction of the spaces of Fontana, by vitreous. He supported this view by the results of experimental injections of vitreous into the anterior chamber of rabbits.

Wickerkiewicz (1904) expressed the view that the condition resulted from retraction towards the periphery of the divided membrane and consequent obstruction of the passage between the posterior and anterior chambers; while evacuation of the anterior chamber might cause the vitreous body to advance so that the membrane might be applied to the iris, and thus to the excretory channels.

Cheney (1909) supported the view that in the majority of these cases glaucoma is due to obstruction of the filtration angle by vitreous which has come forward into the anterior chamber, and to a greater or less extent replaced the aqueous; while at times, when the vitreous puncture has been made at some distance from the pupil, without evacuation of the aqueous, it may be that the vitreous does not come in front of the iris, but pushes forwards a portion of it, thus obliterating temporarily a certain extent of the filtration angle, so interfering with lymph excretion. He pointed out that it might reasonably be supposed that a vitreous of normal consistence would form more of an obstruction in the angle of the anterior chamber than a vitreous which had become partially degenerated, and which would speedily liquefy.

The discrepancy of opinion which is evident from the above *résumé* may to a large extent be accounted for by the fact that apparently no published records of the anatomical conditions in cases of this class exist. The description of the following case may therefore be of interest before an attempt be made to reconcile the various views

which have been expressed as to the ætiology and appropriate treatment of the condition.

Case 9.—Jas. H., *æt.* 59.

The patient was admitted to the R.L.O.H. on January 24th, 1910. The left lens had been removed 24 years previously, probably by discission, as there was no scar of extraction. The sight had been good after operation, but the eye had not been used. The eye had been red and painful since a blow received three months previously.

On admission the left eye was injected. There was bulbous keratitis with corneal haze, but no post-corneal deposits. The pupil was dilated and showed no posterior synechiæ. The tension was + 3, and there was no perception of light. The fundus could not be seen.

The eye was enucleated, fixed in Zenker's fluid, and divided from above in an antero-posterior meridian (Reg. No. 8027).

Macroscopical Appearances.

The lens is absent. A membrane containing very scanty remains of the lens stretches between the ciliary processes. It has a slight convexity forwards, but is everywhere separated from the iris, the interval between it and the peripheral part of the iris measuring about 1·5 mm. There is a large aperture in the centre of this membrane, through which the vitreous projects in a conical process into the anterior chamber. The iris is thick and is adherent by its peripheral part to the tissues forming the anterior boundary of the angle of the anterior chamber. The adhesion, which is more extensive above than below, can be fairly easily separated. The vitreous is consistent in its peripheral part, degenerate centrally, the process which projects forwards into the anterior chamber having a shaggy appearance.

Microscopical Appearances.

The corneal tissues are normal. Both above and below, the iris, with the exception of its peripheral part, is very œdematous, the anterior surface exhibiting deep depressions between high prominences, the most peripheral of which is applied above to the posterior surface of Descemet's membrane and below to the

most central part of the ligamentum pectinatum. This part of the iris is slightly atrophic but shows no evidence of inflammation. Above, the more peripheral part of the iris is applied to the back of Descemet's membrane, the endothelial lining of which is fairly well preserved, and the ligamentum pectinatum, the tissues of which are somewhat compressed but fairly easily distinguishable. The iris tissues here show evidence of some slight atrophy. The channels of Schlemm's canal are somewhat narrowed and the surrounding tissue is hypercellular and contains a considerable number of dense pigment masses. Below, the peripheral portion of the iris is seen in some sections to be applied to the ligamentum pectinatum, while in others it is separated by narrow spaces; its tissues are compressed but not markedly atrophic. The tissues of the ligamentum pectinatum are somewhat compressed and hold a few scattered red blood corpuscles in their meshes, while the channels of Schlemm's canal are normal in appearance. In the false angles of the anterior chamber, at various points on the surface of the iris, and in the cavity of a large crypt in the neighbourhood of the circulus iridis minor below is a dense granular material resembling in consistence and staining character degenerate vitreous. A few red blood corpuscles are also present in the lower false angle.

The ciliary body is free from signs of inflammation. The muscle is very atrophic, while the anterior ciliary processes are also atrophic and are separated by a wide interval from the base of the iris. The posterior processes are normal, and behind them, presenting a slight convexity forwards, lie the remains of a diaphragm with large central defect formed by the suspensory ligament and very scanty lens remnants. Amongst the ciliary processes lies a material similar to that met with on the anterior surface of the iris and in the angles of the anterior chamber, and probably consisting of degenerated vitreous. The vitreous in the situation of its retinal attachment is of fairly normal and consistent character; it contains in its lower part a minute extravasation of blood.

The inner layers of the retina are somewhat atrophic. The choroid is of normal appearance. The optic disc is considerably cupped. The optic nerve, cut in serial sections, shows some

atrophy of the nerve fibres. There is considerable degeneration of the walls of the central vessels just behind the lamina cribrosa, which has not, however, produced occlusion of the lumen.

In this case the anatomical conditions, more especially that of the iris, point to an onset of acute glaucoma of comparatively recent date, probably as the direct result of the injury received three months previously. The increased tension is to be attributed chiefly to a dislocation forwards of the iris so that its root has come to form an extensive obstruction to the excretory channels at the angle of the anterior chamber, and the condition has probably been aggravated by a further obstruction of the excretory channels both here and in the iris by degenerate vitreous. Although it is impossible to speak with certainty on the point, yet in view of the presence of a large opening in the capsular membrane and the free projection through this of vitreous, it seems not unlikely that the injury may have been responsible for a passage forwards of vitreous, which has brought about a forward dislocation of the iris in the same manner as has been described above in some of the cases of complete dislocation backwards of the lens.

The diversity of opinion as to the causation of glaucoma in these cases of discission of after-cataract is probably to be accounted for by the fact that this condition may arise from a variety of causes. Thus there can be little doubt that it may result from an iridocyclitis set up or aggravated by traction on the ciliary processes as hypothecated by von Graefe. This was probably the sequence of events in a case within the writer's experience in which the operation on an eye showing slight signs of cyclitis (circumcorneal flush with recent post-corneal deposits) was followed by further signs of inflammation with fresh deposits and increased intra-ocular tension. In the majority of cases, however, the accident is probably to be referred to injury to the vitreous resulting in its passage forwards against the posterior surface of the iris or through the pupil.

Cases of glaucoma arising in this way may be divided into two distinct classes, in which the difference in the clinical signs is probably dependent on a corresponding difference in the *rationale* of the glaucoma production. Thus it is probable that those cases which are associated with a deep anterior chamber and flat iris are to be explained as the result of passage forwards of vitreous into the anterior chamber, which, by obstructing the excretory channel and so interfering with the normal excretion of fluid, may give rise to increase of tension. To this category would belong cases such as those described by Cheney, and one observed by the writer, in which six hours after discission of after-cataract a condition of subacute glaucoma with deep anterior chamber supervened, but completely subsided within a few hours under the influence of eserine with hot applications. In this case signs of inflammation were absent, while the vitreous was known to be of abnormally fluid consistence. It is probable that the liability of the vitreous to pass into the anterior chamber is increased by an abnormal fluidity such as existed in this case and in the four cases of a series of 40 myopic eyes in which the same complication was noted by Bronner. On the other hand, it is likely that the more consistent the vitreous tissue, the greater will be the disturbance caused by its presence in the angle of the anterior chamber. Thus the writer has observed a condition of very considerable abrupt increase of intra-ocular tension with deep anterior chamber and without inflammatory phenomena in the eye of a man aged 22, the subject of a severe contusion received rather more than six months previously. The lens, which was tremulous after the accident, had become almost completely absorbed after three discission operations, and the glaucoma was attributed to the presence in the anterior chamber of vitreous probably of good consistence. The prompt relief of symptoms afforded by the use of eserine and heat suggested that the drug had acted not only by producing an increased patency of the excretory channels, but also by bringing about as

a result of contraction of the pupil a centripetal traction on strands of vitreous obstructing the passages at the angle of the chamber.

On the other hand, it is not unlikely that in some cases, where a free discission has been made, the vitreous may by its passage forwards exert a forward pressure on the iris, and thus give rise to a narrowing or obstruction of the chamber angle, while it is probable that in those cases in which the glaucomatous attack is associated with a bombé condition of the iris (*cf.* Bowman, Knapp), the condition is to be attributed to a hernia-like protrusion of the vitreous through the pupil, which, by overlapping of, or actual adhesion to, the pupillary border, causes an obstruction to the perfectly free passage of fluid from posterior to anterior chamber, and thus leads to over-distension of the former. Such a forward passage of vitreous would obviously be favoured by evacuation of the aqueous at the time of operation. The supposition as to its occurrence and significance receives support from the anatomical findings in some of the cases of glaucoma associated with complete backward dislocation of the lens, which have been described in the earlier part of this paper.

The difficulty in reconciling the various lines of treatment recommended by different authors to a large extent vanishes with a recognition of the variety in the anatomical conditions which may be responsible for the increased intra-ocular tension in these cases. On broad lines, it may be stated that, apart from those cases in which the glaucoma is dependent on a direct pressure forwards of the iris by lens and vitreous, as in some cases of subluxation of the lens, or on a condition of iridocyclitis in which the appropriate treatment on general principles is indicated, treatment will be directed along one of two different lines according as the condition is the result of direct obstruction to the excretory channels, or is due to a forward position of the iris root. Thus, a condition of glaucoma, with deep anterior chamber, dependent on obstruction to excretion of fluid from the anterior chamber will afford an indication

for the use of a myotic (*cf.* Knapp, Cheney), with a view to opening up the excretory channels. The effect of the drug may be aided by heat, and will be found in many cases to be strikingly successful; if unsuccessful, it may be followed by paracentesis of the anterior chamber and evacuation of the contained vitreous (*cf.* Cheney). The persistence of glaucoma after such measures would be most suitably treated by an attempt to establish a leaking cicatrix, *e.g.*, by Herbert's sclerotomy.

When, on the other hand, the glaucoma is dependent on direct pressure forwards of the iris by vitreous, or on a bombé iris consequent on obstruction of the pupil, an attempt may be made to relieve the condition by the use of a mydriatic (*cf.* Bowman, "Atropine should certainly be used"). If this be not speedily successful, it will be necessary in a case of bombé iris to establish a communication between the anterior and posterior chamber by means of an iris puncture (Bowman) or iridectomy (Knapp). The former procedure has the advantage of simplicity, but will be contra-indicated, except as a palliative measure, in those cases in which the glaucoma is of any considerable standing, and has resulted in an adhesion of the iris base to the corneo-sclera, a condition which can only be efficiently treated by a peripheral iridectomy. On the other hand, if iridectomy be selected as the procedure in a glaucoma of recent onset, the ideal operation would appear to be one which, while removing the base of the iris, would leave the sphincter intact, and thus give rise to a minimum disturbance of the vitreous. Such, however, is not likely to be easily executed in practice, owing to the difficulty in manipulating the iris in these cases with any instrument except a hook. A condition of glaucoma due to a direct pressure forwards of the iris by the vitreous will also afford an indication for iridectomy. Should the glaucoma persist, an attempt must be made to establish a leaking cicatrix, *e.g.*, by means of Herbert's sclerotomy.

In the treatment of glaucoma associated with sub-

luxation of the lens, and due to a pressure forwards of the iris by the lens on one side and the vitreous on the other, the choice of procedure will lie between the exceedingly precarious operation of scoop extraction of the lens, iridectomy at the opposite side to the lens displacement, and Herbert's sclerotomy.

An important point in the subject of the supervention of glaucoma, after the discission of after-cataract, relates to prophylaxis, in view of the greater liability to the supervention of this complication afforded, on the one hand, by extensive laceration of the vitreous, and on the other by evacuation of the anterior chamber. This point has been emphasised by Bowman, Knapp, and Cheney. The space lying between the capsular membrane and the vitreous, and filled by lymph, which is hypothecated by Cheney, probably never exists apart from pathological conditions affecting the anterior part of the vitreous, and any excursion of the needle or knife behind the membrane must therefore result in injury to the vitreous. As has already been pointed out, the extreme anterior part of the vitreous is usually of fairly firm consistence, and superficial injuries will therefore not result in any great disturbance of the tissues. Any unnecessary laceration is, however, strongly to be deprecated, in view of the liability to the glaucomatous complication. On this account there is, in the writer's opinion, much in favour of the procedure of dividing any but the most delicate membranes with a Ziegler's knife, which is made to penetrate the membrane with extreme obliquity, insinuated between it and the most anterior part of the vitreous, and made to divide the former in a forward direction by a gentle sawing movement. The opening may be subsequently enlarged in an upward or downward direction. The temptation to divide dense bands, when it is possible to make an efficient opening in a more delicately constituted area, must be rigorously foregone, as likely to lead not only to a disappointing result as regards vision, but also to serious complications, consequent on undue traction on the ciliary

processes or laceration of the vitreous. An escape of aqueous is most efficiently safeguarded by an oblique entry of the discission instrument immediately behind the limbus.

Bibliography.

Complete Posterior Dislocation of the Lens.

Lawford. Roy. Lond. Ophth. Hosp. Rep., 1887, vol. xi, p. 330.
Straub. Arch. f. Ophth., 1888, vol. xxxiv, 3, p. 195.

Subluxation of the Lens.

Alt. Amer. Journ. of Ophth., February, 1896.
Collins. Catalogue of Museum, Roy. Lond. Ophth. Hosp., 1893, p. 135.
Ischreyt. Arch. f. Augenh., 1901, vol. xlii, p. 281.
Lawford. Roy. Lond. Ophth. Hosp. Rep., 1887, vol. xi, pp. 327 and 329.
Priestley Smith. Ophth. Rev., 1883, vol. ii, p. 257.
Terson. Arch. d'Opht., vol. xiv, p. 340.

Discission of After-Cataract.

Averbach. Wratoch., 1, Nos. 52 and 53.
Bayardi. R. Acc. di med. di Torino, 1896.
Bernheimer and Hirsch. Wien. klin. Woch., 1898, pp. 17, 28, and 29.
Bowman. Roy. Lond. Ophth. Hosp. Rep., 1865, p. 332.
Brailey. Roy. Lond. Ophth. Hosp. Rep., 1879, p. 379.
Bronner. Brit. Med. Journ., 1902.
Buller. Trans. Am. Ophth. Soc., 1891, vol. vi, p. 120.
Cheney. Ophthalmology, 1909, vol. v, p. 27.
Dalen. Mittheil. aus der Carolinisch. Institut zu Stockholm, 1901, p. 75.
Dupuy-Dutemps. Ann. d'Oc., 1904, vol. cxxxii, p. 93.
v. Graefe. Arch. f. Ophth., 1869, vol. xv, 3, p. 108.
Heymann. Klin. Mon. f. Augenh., 1867, p. 147.
Knapp. Arch. f. Augenh., vol. xxx, p. 1.
Linnell. Journ. Ophth., Ot. and Laryng., 1892, vol. iv.
Natanson. Ueber Glaukom in aphakischen Augen. Dorpat, 1889.
Pagenstecher. Klin. Mon. f. Augenh., 1895, p. 139.
Rennecke. Inaug. Dissert. Berlin, 1894.
Risley. Am. Journ. Ophth., 1899, p. 328.
Voigt. Arch. f. Ophth., vol. liv, p. 227.
Wickerkiewicz. Ann. d'Oc., 1904, vol. cxxxii, p. 5.